

## COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING HIV INFECTION

This application claims the benefit of U.S. Provisional Application Nos.

5 60/491,258 filed July 31, 2003, 60/493,767 filed August 11, 2003, 60/496,908 filed  
August 22, 2003, and 60/501,832 filed September 11, 2003, which are hereby  
incorporated by reference in their entirety.

## BACKGROUND OF THE INVENTION

10 Acquired Immune Deficiency Syndrome (“AIDS”) is one of the most serious  
health threats confronting the human population today. AIDS is caused by a virus  
known as human immunodeficiency virus (“HIV”) which presently includes HIV-1  
and HIV-2. Over 40 million people are estimated to be living with HIV/AIDS.  
Current projections suggest that an additional 45 million people will become infected  
15 between 2002 and 2010. So far, it is believed that more 25 million people have died  
from AIDS.

Since its emergence in the 1970s, HIV has produced a continually growing  
global pandemic, and it has, thus far, defied all attempts to produce an effective  
vaccine. Although a number of drugs have been developed to treat the disease, all  
20 have limited usefulness, serious side effects, a high potential for resistance, and none  
have been identified so far which can cure or prevent it. HIV vaccine research has  
expanded over recent years, but success so far using HIV-based components has been  
limited. See, e.g., Graham et al., *J. Inf. Disease.*, 166:244-252, 1992; Belshe et al., *J.*  
*Inf. Disease.*, 183:1343-52, 2001; Horton et al., *J. Virol.*, 76:7187-7202, 2002; Gilbert  
25 et al., *Vaccine*, 21:2933-2947, 2003.

## DESCRIPTION OF DRAWINGS

FIG. 1 (A-C). Comparison of cells from vaccinated versus non-vaccinated subjects,  
infected with the macrophage (CCR5) tropic HIV. A. A comparison of the mean +  
30 standard error measurement of the vaccinated versus non-vaccinated groups in  
cultures without autologous serum. (\*, p<0.05) B. A comparison of the mean +

standard error measurement of the vaccinated versus non-vaccinated groups in cultures with autologous serum (\*, p< 0.05; \*\*, p<0.01). C. Comparison of the mean + standard error measurement of cells from vaccinated versus non-vaccinated subjects, infected with the T-cell (CXCR4) tropic HIV.

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### DESCRIPTION OF THE INVENTION

The present invention provides methods and compositions for treating and/or preventing HIV infection in a subject in need thereof. It features the use of poxviruses for therapy, prophylaxis, and diagnosis of HIV, as well as for any other 10 medical or veterinary use associated with HIV and homologous viruses. The invention also provides for the use of poxviruses in the discovery of new agents to prevent and/or treat HIV infection.

A poxvirus or a component thereof, can be used to treat and/or prevent infection caused by any virus, preferably a lentivirus, such as HIV, that uses a CCR5 15 chemokine receptor for its infection of cells. This includes, but is not limited to, e.g., HIV-1 (e.g., clades A, B, C, D, and G, R5 and R5X4 viruses, etc.), HIV-2 (e.g., R5 and R5X4 viruses, etc.), simian immunodeficiency virus (SIV), simian/human immunodeficiency virus (SHIV), feline immunodeficiency virus (FIV), bovine immunodeficiency virus (BIV) (Wright et al., *Vet. Res. Commun.*, 26:239-50, 2002), 20 HTLV-1, HTLV-2, etc. It can be used as a vaccine, adjuvant, therapeutic agent, in combination with other agents, or in any suitable manner to treat and/or prevent such infections.

Any poxvirus can be used in accordance with the present invention, including, but not limited to, orthopoxvirus, parapoxvirus, avipoxvirus, capripoxvirus, 25 leporipoxvirus, suipoxvirus, etc. Orthopoxvirus, include, e.g., buffalopox, camelpox, cowpox, monkeypox, rabbitpox, raccoon pox, tatera pox, canarypox, fowlpox, vaccinia, variola, and vole pox. Vaccinia virus is the prototype of the genus Orthopoxvirus for the desired effects, but other poxviruses can be used in its place. Thus, although the disclosure below may be written in terms of vaccinia, any poxvirus 30 can be utilized in accordance with the present invention.

Vaccinia is a double-stranded DNA (deoxyribonucleic acid) virus. All strains, derivatives, variants, mutations, naturally-occurring strains, genetically-engineered, recombinant, etc., of vaccinia can be used in accordance with the present invention.

For more information on vaccinia and other poxvirus, see e.g., *Virology*, Fields et al.,

5 Volume 2, Chapters 74-75, Raven Press, 1990.

An amount of the poxvirus, such as vaccinia virus, can be administered to a subject in a quantity which is effective to achieve a therapeutic or prophylactic effect. The term "poxvirus," "vaccinia virus," etc., indicates that the virus (genome and protein coat) is administered to a subject. It can be administered in any effective 10 form, including, e.g., as a live virus, as a live-attenuated virus, as a replication-deficient virus, as a viral extract not having any live viral particles, etc. Compositions comprising a poxvirus can be produced and utilized in any suitable manner, including, e.g., recombinant, naked DNA technology, etc.

The term "treating" is used conventionally, e.g., the management or care of a 15 subject for the purpose of combating, alleviating, reducing, relieving, improving, eliminating, etc., one or more signs or symptoms associated with HIV infection. Treatment includes delaying the progression of HIV and its associated symptoms, thereby extending the life expectancy of an infected subject, and/or delaying or reducing the onset of symptoms associated with HIV infection. Treating can involve 20 inhibiting, reducing, diminishing, etc., the replication and other events in the life cycle of the HIV virus.

The term "preventing" HIV infection indicates that a subject's susceptibility to HIV infection upon exposure to the virus is reduced or diminished as a result of the administration of the poxvirus. The subject's resistance to HIV infection is increased 25 or improved by the poxvirus treatment since s/he is less likely to become infected by the virus. Any amount of improved resistance is useful, e.g., greater than 5-fold, greater than 7-fold, greater than ten-fold, etc., and any such improvement can be regarded as prevention.

A poxvirus, or component thereof, used in the present invention can be 30 prepared routinely, or obtained from commercial sources. Attenuated strains are preferred. Attenuated strains are less able to cause disease, and are considered less virulent and weakened as compared to strains that are not attenuated.

Any strain of vaccinia virus, or components thereof, can be utilized to achieve a prophylactic and/or therapeutic effect, including, but not limited to, e.g., strains available from the ATCC, ECACC, or other virus collections, replication-competent, replication-deficient, non-replicating, attenuated strains, modified vaccinia Ankara (MVA), vaccinia virus Ankara, NYVAC (ATCC No. VR-2559) replication-deficient vaccinia viruses, VV Copenhagen, VV Western Reserve, VV Wyeth (ATCC No. VR325), Elstree, strains deficient in vCCI (Reading et al., *J. Immunol.*, 170:1435-42, 2003), and/or vGF, strains comprising one or more copies of the 17K myristyloprotein, poxvirus strains, CCR5-dependent poxvirus strains, etc. Dryvax®, a vaccinia (smallpox) vaccine currently licensed in the United States, is a lyophilized, live-virus preparation of infectious vaccinia virus (Wyeth Laboratories, Inc., Marietta, Pennsylvania). Other strains which have been used include, but are not limited to, e.g., Lister, Bordeaux, Paris, Massachusetts 999, New York, Temple of Heaven, Patwadangar, Ikeda, Bern, Vienna, Bohemia, Finland, Hamburg, Budapest, Aosta, Spain, Sweden, B-51, Tashkent, EM-63, LE-IVP (Lister), etc. See, also, *Smallpox and its Eradication*, Fenner et al., WHO, Geneva, 1988, e.g., Chapter 11. Other strains include, e.g., MVA-BN (modified vaccinia Ankara – Bavarian Nordic) (ECACC V00083008; WO 02/42480), MVA-Vero (US 20030013190), MVA-NH, MVA 572 (ECACC V94012707), LC16m8, and ACAM1000 (ATCC Deposit No. PTA-3321; WO 02/085411). Any strain of canarypox can be utilized as well, including attenuated canarypox virus such as, e.g., ALVAC (ATCC No. VR-2547).

Deposited strains also include, e.g., ATCC Nos. VR-117 (CL), VR-118 (Lederle-Chorioallantoic), VR-119 (WR (Mouse Neurotropic), VR-1354 (WR (NIH TC-adapted), VR-1431 (P-4), VR-1441 (IHD-W), VR-1508 (Modified vaccinia virus Ankara (MVA)), VR-1536 (New York City Department of Health Laboratories (Wyeth-calf adapted)), VR-1549 (Elstree (Lister Vaccine)), VR-156 (IHD), VR-2010 (AS), VR-2031 (Vtk-79), VR-2034 (S-variant), VR-2042 (vP-7), VR-2043 (vP-9), VR-2292 (SLZ103[recombinant Vaccinia virus (WR)]), VR-2379 (Rpmuhr+ [recombinant of Utrecht strain Rpuhr23]), VR-2589 (VVtm1:hPC1 [recombinant Vaccinia virus, in vitro construct]), VR-302 (Brighton), VR-3103 (IHD-W Dts 16 [Vaccinia ts-mutant]), VR-3109 (IHD-W Dts 46 [Vaccinia ts-mutant]), VR-3110 (IHD-W Dts 2 [Vaccinia ts-mutant]), VR-3113 (IHD-W Dts 17 [Vaccinia ts-mutant]),

VR-3121 (IHD-W Dts8 [Vaccinia ts-mutant]), VR-3126 (IHD-W Dts 33 [Vaccinia ts-mutant]), VR-3129 (IHD-W Dts 48 [Vaccinia ts-mutant]), VR-3130 (IHD-W Dts 4 [Vaccinia ts-mutant]), VR-3139 (IHD-W Dts 50 [Vaccinia ts-mutant]), VR-3142 (IHD-W Dts 10 [Vaccinia ts-mutant]), VR-3144 (IHD-W Dts20), VR-3147 (IHD-W 5 Dts 35 [Vaccinia ts-mutant]), VR-3148 (IHD-W Dts 40), VR-3154 (IHD-W Dts71 [Vaccinia ts-mutant]), VR-3160 (IHD-W Dts52 [Vaccinia ts-mutant]), VR-3161 (IHD-W Dts 57), VR-3165 (IHD-W Dts 77), VR-3166 (IHD-W Dts 82), VR-3169 (IHD-W Dts97 [Vaccinia ts-mutant]), VR-3175 (IHD-W Dts 78 [Vaccinia ts-mutant]), VR-3176 (IHD-W Dts 83 [Vaccinia ts-mutant]), VR-3178 (IHD-W Dts 93 10 [Vaccinia ts-mutant]), VR-3196 (IHD-W Dts 95 [Vaccinia ts-mutant]), VR-587 (Yaba monkey tumor virus deposited as Yaba monkey tumor virus, Yatapoxvirus (Roswell Park-Yohn)), VR-838 (Raccoonpox virus, Orthopoxvirus (Herman)).

A vaccinia virus is a preferred poxvirus in accordance with the present invention, but other poxviruses can also be used to treat and/or prevent HIV. For 15 example, any poxvirus which expresses a gp120-like or TAT-like polypeptide, or which depends on CCR5 for entry into a cell can be used in accordance with the present invention.

Vaccinia virus can be administered to subjects according to any regimen which is effective for treating and/or preventing HIV infection. The particular 20 dosages (i.e., effective amounts), and number and frequency of vaccinations can be determined routinely.

An effective amount of virus, or virus component, is the quantity of virus, or virus component, which is useful to achieve the desired purpose, e.g., to treat and/or prevent HIV infection. These amounts can be determined routinely. Effective 25 amounts can be the same or less than the amounts currently used to achieve pox immunity with a pox vaccine. For example, Dryvax™ is commonly used at a potency of 100 million pock-forming units (pfu)/ml for primary vaccination for smallpox. Any effective amount can be used in accordance with the present invention, e.g., about  $10^5$ - $10^9$  pfu/ml. The quantities of the particular virus which is utilized can be 30 adjusted and determined routinely, e.g., to eliminate or reduce adverse reactions associated with the virus, as well as depending on the health of the patient receiving the treatment.

The specific dose level and frequency of dosage may vary, and can depend upon a variety of factors, including the activity and state of the specific poxvirus, e.g., whether it is live, heat-inactivated, attenuated, etc., its metabolic stability and length of action, rate of excretion, mode and time of administration, and the age, body 5 weight, general health, gender, diet, and particular condition of the subject undergoing treatment or prevention.

Poxvirus can be administered in any form by any effective route, including, e.g., oral, parenteral, enteral, intraperitoneal, topical, transdermal (e.g., using any standard patch), ophthalmic, nasally, local, non-oral, such as aerosol, spray, 10 inhalation, percutaneous (epidermal), subcutaneous, intravenous, intramuscular, buccal, sublingual, rectal, vaginal, intra-arterial, mucosal, and intrathecal, etc. It can be administered alone, or in combination with any ingredient(s), active or inactive.

Any subject can be administered a poxvirus in accordance with the present 15 invention, including subjects who have been exposed to HIV, but have not yet developed HIV infection, as well as subjects who have progressed to one or more of the clinical symptoms of HIV infection (e.g., AIDS). In addition to treating and/or preventing HIV infection in humans, a poxvirus can be used to treat other organisms (e.g., non-human primates, cats, etc.) infected with HIV, or HIV-related viruses, such 20 as SIV, SHIV, or FIV. Thus, subjects who can be treated include, e.g.; mammals, humans, monkeys, apes, chimpanzees, gorillas, cats, dogs, mice, rats, etc.

Subjects, who have been exposed to HIV virus, or who are at risk for developing the disease, are particular candidates for poxvirus vaccination. For instance, a subject who has not yet tested positive, but has been exposed to HIV, can 25 be administered vaccinia virus as a prophylactic/therapeutic approach. Individuals at high-risk for the disease, such as sexually-active individuals, subjects in parts of the world where HIV infection is high, subjects receiving blood and/or other invasive medical procedures, can also receive vaccination to increase their resistance to HIV infection.

30 In addition to administering the whole poxvirus, components of it can also be administered in accordance with the present invention. By the phrase "component," it is meant any part of the virus, which is less than the whole virus genome, including

particular nucleic segments of its genome, as well as any product which is produced using the viral genome. This includes modifications to polypeptides encoded for by the virus.

Components include polypeptides comprising the virus, such as envelope 5 proteins, processing enzymes, structural proteins, nucleic acid synthesis enzymes, glycoproteins, carbohydrates, lipids, antigens or antigenic fragments of the virus, etc. Also included are nucleic acid fragments of the whole genome, including fragments comprising complete gene sequences, control sequences, etc.

Components includes one or more of the over about 198 open reading frames 10 (ORF) and about 268 genes that have been identified in vaccinia and other poxvirus. Components include one or more of the genes and products thereof described in, but not limited to, Antoine et al., *Virology*, 244:365-396, 1998, and Goebel et al., *Virology*, 179(1):247-266, 1990 for vaccinia virus; Willer et al., *Virology*, 264(2):319-43, 1999 for Leporipoxvirus Shope fibroma virus (SFV); Cameron et al., *Virology*, 15 264(2):298-318, 1999 for myxoma virus; Shchelkunov et al., *Virology*, 297(2):172-94, 2002 for monkeypox virus; Shchelkunov and Totmenin, *Virus Genes*, 9(3):231-45, 1995 for variola, Massung et al., *Virology*, 201(2):215-40, 1994. For example, the polypeptide coding for the 17K myristylprotein, and which has amino acid sequence homology to gp120, can be used alone or in combination with other antigens, etc., in 20 accordance with the present invention. See, e.g., Antoine et al., 1998; Barrett et al., *Seminars in Immunol.*, 13:73-84, 2001. See, also Tables 1 (from Goebel et al., *Virol.*, 179:247-266, 1990) and 2 (from Antoine et al., *Virol.*, 244:365-396, 1998). Moreover, one or more of the aforementioned genes and open reading frames can be deleted 25 from a vaccinia virus, e.g., to eliminate a toxic or other undesirable effect of an administered virus.

A useful composition can comprise one of the components of a poxvirus, including one or more of the components described in Tables 1 and 2. These can be individual purified and then combined into a therapeutic or prophylactic composition, or extracts can be prepared from viral particles and treated as desired. The individual 30 components can be purified from the viral particles, or produced recombinantly, e.g., where a target gene is cloned, expressed in a host cell under conditions where the polypeptide is manufactured by the cell, and separating and purifying the polypeptide

accordingly to conventional methods. Components can also be administered as naked DNA. See, e.g., U.S. No. 6,413,942.

The therapeutic and/or prophylactic effect achieved with the poxvirus can be independent of an immunological response to it. For example, the purpose of 5 ordinary smallpox vaccination is to elicit an immune response by the host. This response is both humoral and cellular, involving the generation of specific antibodies and immune cells (such as T-cells, cytolytic or cytotoxic T lymphocytes, etc.) which protect a host from future invasion by the smallpox virus. While the present invention is not bound by any mechanism through which the poxvirus achieves its therapeutic 10 and/or prophylactic effect, it can be mediated through a pathway separate from the immune response and not require cellular or humoral immunity. For example, poxvirus, or a component thereof, can directly block or inhibit the ability of a HIV to infect a cell. In this respect, the poxvirus, or component of it, acts as an antagonist, blocker, etc., of HIV's ability to infect target cells. HIV usually activates a G-protein- 15 coupled signal pathway cascade. Poxvirus can interfere with this pathway or modify it such a way that the cell is more difficult to infect, thereby increasing its resistance to the HIV virus. Consequently, the effective amounts of a poxvirus, or component thereof, can differ from the amounts that are ordinarily used when the objective is to achieve a humoral and/or cellular immune response.

20 Vaccination with vaccinia can be associated with adverse reactions. Those at highest risk include, e.g., pregnant women, immunocompromised patients (e.g. HIV- positive), and persons who have atopic dermatitis or eczema. Strains which are attenuated or otherwise modified to reduce adverse effects are especially useful in accordance with the present invention, e.g., for administration to persons at risk for 25 adverse effects.

Modified strains of vaccinia can be utilized that are deficient, mutated, engineered, etc., in one or more of the about 198 open reading frames (ORF) and/or about 268 genes that comprise vaccinia (depending on the strain or variant). In addition, genes can be inserted into vaccinia, including, one or more copies of a 30 vaccinia gene of interest (e.g., 17K myristylprotein, vCCI), and/or genes coding for all or part of an HIV proteins, such as gp120 or gp40.

The present invention also provides methods of treating and/or preventing HIV infection in a subject in need thereof, comprising, e.g., administering multiple doses of a poxvirus, or components thereof, to a subject, wherein each dose is administered at a time interval from the previous dose, and are effective to maintain a therapeutic effect, or to maintain protection against HIV infection. As discussed above, a dose of the poxvirus, or component thereof, is the amount of virus which is useful for accomplishing the therapeutic or prophylactic effect. More than one dose can be administered to the subject in order to maintain the therapeutic efficacy of the treatment, or to maintain protection against HIV infection. For example, smallpox immunization is usually achieved by a single vaccination with a booster every 5-10 years. To maintain protection against HIV, more frequent vaccination can be used, e.g., multiple times a year, at least twice a year, yearly, every two years, every three years, more than once every less than five years, more than once every less than ten years, etc. The periods between the separate and sequential vaccinations can be referred to as "time intervals." These intervals can be spaced apart by any desired time period which is effective to maintain protection or therapeutic efficacy in treating an infected subject. The intervals can be predetermined or preset, where they are already specified, or they can be determined by monitoring the progress of a subject, e.g., using blood serum to measure poxvirus antibody titer, or HIV titer in an infected subject. The frequency of vaccination utilized to achieve efficacy may vary depending upon multiple factors, including, e.g., person-to-person variations in the immune system, the stage of HIV infection, the potency of the virus or vaccine, etc., and may be as often as every 3 months to once every 5 years.

The present invention also provides methods of treating and/or preventing lentivirus infection in a subject in need thereof, comprising: administering an effective amount of a poxvirus or component thereof, wherein said amount is effective to treat and/or prevent lentiviral infection, with the proviso that a lentivirus nucleic acid, such as HIV, is not contained in the poxvirus genome. This excludes, e.g., a poxvirus which is utilized as a vector to administer HIV nucleic acid, such as when HIV nucleic acid is inserted into the poxvirus genome.

The present invention also provides methods of identifying a component of a poxvirus, or a poxvirus-associated agent, which interferes with HIV infection, and

components and agents identified thereby. Interfering with HIV infection indicates that the agent or component decreases, reduces, diminishes, lessens, etc., the ability of a susceptible cell or organism to become infected with HIV virus as compared to the same cell or organism in the same conditions, but in the absence of the agent or 5 component. Interference with HIV infection can occur at any level, e.g., by blocking the ability of HIV to attach to its receptor(s) on a cell, by blocking the ability of HIV to be taken into a cell, by blocking viral function once inside the cell, by blocking viral infection, etc. The invention is not limited by the mechanism through which HIV interference is achieved. By interfering with HIV infection, the cell's or 10 organism's resistance to HIV is increased.

These methods can involve one of more of the following steps in any effective order, e.g., (1) contacting a cell or organism which is susceptible to HIV infection with poxvirus, or a component thereof, or a poxvirus-associated agent, (2) contacting said cell or organism with HIV under conditions effective for said HIV to infect said 15 cell or organism, and, (3) (a) determining whether said cell or organism is resistant to HIV infection, whereby said agent is identified as interfering with HIV infection, or (3) (b) identifying the poxvirus, or component thereof, which confers resistance to HIV infection. The term "organism" as used herein indicates a fully-gestated animal.

The method can also involve a step of identifying the poxvirus, or a 20 component thereof, as the agent which confers resistance to HIV infection. Identifying the poxvirus, or component thereof, which confers resistance to HIV infection, indicates that the poxvirus is positively determined or ascertained to provide protection or resistance against HIV. This indicates a positive result in the method.

25 Agents can be tested for their ability to interfere with HIV infection in any suitable system, including whole animals and cell culture. Animal cells useful in the present invention are those which are susceptible to HIV infection, i.e., they are capable of being infected by the HIV virus. They can be naturally-susceptible, or genetically-engineered to confer susceptibility, e.g., by expressing HIV receptor 30 (CCR5, CD4, etc.), or by grafting on the human immune system. Any methods for testing whether a cell or organism is infected with HIV can be used, e.g., measuring

anti-HIV antibody titer (e.g., gp120 antibodies), reverse transcriptase protein or nucleic acid, or any other polypeptide or nucleic acid.

Any suitable animal model for testing the efficacy and dosage of a poxvirus (or component thereof) can be used in accordance with the present invention. These 5 include, but are not limited to, e.g., SCID mice reconstituted with human immune system components (e.g., peripheral blood lymphocytes) [e.g., Zhang et al., *Proc. Natl. Acad. Sci.*, 93:14720-14725, 1996, using SCIC.bg mice], chimpanzees infected with HIV-1, macaque monkeys infected with SIV, HIV2, or chimeric SIV/HIV [e.g., Johnson, *Curr. Opin. Immunol.*, 8(4):554-560, 1996], cats infected with feline 10 immunodeficiency virus, HIV-1 transgenic mouse model [e.g., mice which have integrated molecular clone pNL4-3 containing 7.4 kb of the HIV-1 proviral genome deleted in the gag and pol genes (Dickie et al., *Virology*, 185:109-119, 1991; transgenic mice carrying an HIV provirus, optionally with deletion of one or more HIV genes (Tinkle et al., *J. Clin. Invest.*, 100(1):32-9, 1997)], HIV-1 transgenic rat 15 model, human CD4 transgenic rat model, horse infected with EIAV, sheep infected with visna virus, goats infected with CAEV, etc. See, also, *The Retroviridae*, J. A. Levy, ed., Plenum Press, 1993, e.g., Chapters 3, 4, and 5.

A vaccinia virus-associated agent is any substance which is produced in response to a vaccinia infection, or in response to inhalation, injection, ingestion, etc., 20 of any vaccinia virus, or component thereof. This substance can be present in a culture medium in which cells exposed to vaccinia have been cultured, or can be present in blood serum when harvested from an organism exposed to vaccinia. The present invention provides compositions which comprise such substances.

The invention also provides combinations of pharmaceutical agents for 25 treating and/or preventing HIV, e.g., poxvirus, or a component thereof, and an agent which is used to treat HIV, such as a protease inhibitor or a reverse transcriptase inhibitor. Examples of the latter classes of drug, include, but are not limited to, saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, lopinavir, atazanavir, fosamprenavir, tipranavir, AZT, ddI, ddC, ddT, 3TC, nevirapine, delavirdine, etc. 30 The active agents can be present in the same dosage unit (e.g., a composition), or can be used as separate dosage units.

In addition, a poxvirus, such as vaccinia, can be administered in combination with HIV nucleic acid. The HIV nucleic acid can be physically joined to the poxvirus genome, or it can be administered as a separate component. For example, HIV nucleic acid (e.g., coding for gp120 or another viral antigen) can be administered at 5 the same time as a poxvirus, but as a physically separated entity, or it can be administered at subsequent times after receiving only poxvirus) as part of a regimen for treating and/or preventing HIV infection.

The present invention also provides methods of making a poxvirus composition for conferring resistance to HIV infection or treating HIV infection, , 10 comprising, one or more of the following steps in any effective order, e.g., preparing a composition comprising poxvirus, or a poxvirus component thereof, and/or identifying that the poxvirus, or component thereof, confers resistance to, or treats, HIV infection. As mentioned earlier, the identifying step indicates obtaining a positive result in finding that the poxvirus (e.g., vaccinia), or component thereof, 15 provides resistance, protection, treatment, etc., against the HIV virus.

The preparation of a poxvirus composition can be carried out routinely, e.g., according to conventional methods used for vaccine manufacture. Preparing includes culturing poxvirus, isolating poxvirus, putting poxvirus into a form suitable for administration (oral, injection, nasal, etc.), making poxvirus components 20 recombinantly, etc. The prepared poxvirus (or components of it) can be assayed for its ability to confer resistance to HIV infection to an organism challenged with it or provide a therapeutic effect. By this, it is meant that a sample of the prepared composition is tested to determine its titer, concentration, potency, etc., in making a subject, to whom it is administered, "resistant" to the HIV virus, or for its therapeutic 25 effect. The assay step can be carried out on every batch, or only selected batches, etc. A purpose of this step is, e.g., to confirm that the manufactured poxvirus possesses an anti-HIV activity for which it is to be administered. Any suitable assay or testing method can be utilized, e.g., in vitro methods of evaluating its efficacy or potency. For instance, the determining step can involve, e.g., challenging said organism, or 30 cells derived from it, with infectious HIV, and detecting the expression in said organism or cells of gp120, HIV reverse transcriptase, p24, infectious HIV particles, and/or HIV nucleic acid. By "challenge" it is meant the cells or organism are placed

in contact with the HIV virus under conditions which are effective to become infected by it. These conditions will vary, depending upon how the assay is specifically accomplished.

When poxvirus is administered to a host, it can elicit a cellular response that is 5 responsible or associated with the host's subsequent ability to resist HIV infection and/or treat HIV infection. This response can be measured, and used as index or marker to assess the efficacy of the poxvirus, and/or to determine effective amounts of it for the desired purpose (i.e., treating or preventing HIV infection). The 10 appearance of one or more of the following "markers" can be modulated (e.g., elicited, stimulated, down-regulated, up-regulated, etc) by poxvirus, and associated with its anti-HIV effect, thereby making the marker useful as an indicator of poxvirus efficacy. By the term "marker," it is meant any measurable response to a poxvirus, including its effect on HIV's ability to infect and replicate in a cell, as well as on the host's immune system and the cells which comprise it. These markers, include, but 15 are not limited to, one or more of the following agents, activities, responses, pathways, etc.:

- CD4 expression, e.g., measuring the amount of CD4 present in a cell-type that is susceptible to HIV infection
- HIV coreceptor expression, e.g., CCR5 or CXCR4 chemokine receptor, 20 including its cell-surface expression
  - Cytokine receptors
  - Virus-specific CTLs (cytolytic or cytotoxic T-cells, including CD8+ T-cells) which are capable of lysing HIV infected cells (cells can be co-infected with poxvirus and HIV, or infected by HIV alone)
- CD8 cells
- Cytokines, including mediators and regulators of innate immunity, such as interferons, type I interferon, interleukins, interleukin-15, interleukin-12, tumor necrosis factor, interleukin-1, interleukin-6, interleukin-10, etc.; and mediators and regulators of specific immunity, such as interleukins, interleukin-2, interleukin-4, 30 transforming growth factor-beta, interferon-gamma, lymphotoxin, interleukin-5, etc.
- Chemokines (a large family of structurally homologous cytokines, that, e.g., stimulate leukocyte motility and directed movement), including, but not limited to,

the C-C and C-X-C families. Examples of chemokines, include, but are not limited to, e.g., interleukin 8, Gro, platelet basic protein, epithelial-derived neutrophil attractant 78, platelet factor 4, interferon-gamma-induced protein 10, stromal cell-derived factor-1, monocyte chemotactic proteins 1, 2, and/or 3, RANTES, monocyte inflammatory protein 1-alpha and 1-beta ("MIP"), eotaxin, lymphotaxin, etc.

- Th1/Th2 phenotype and cytokine secretion pattern. Effector T-cells (e.g., CD4+ helper T-cells) can be categorized, on the basis of the cytokines they secrete, into Th1 and Th2 cells. Th1 cells secrete, e.g., interferon-gamma, lymphotaxin-alpha, TNF-beta, IL-2, IL-10, and CCR5 ligands, such as RANTES and MIPs. Th2 cells secrete, e.g., IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, etc. Th1 and Th2 cells also include resting, but polarized T-cells (i.e., committed to a Th type). In addition to cytokine production profiles, there are a number of cell surface markers that can be used to differentiate between Th1 and Th2 subtypes. For example, Th1 cells express both components of IL-12 receptor chains (beta1 and beta2), while Th2 cells exhibit IL-12R-beta1. Th2 cells exhibit both IFN-gamma receptor chains (a and b), while Th1 cells express IFN-gamma-R-alpha. Th2 cells appear to express a fully functional IL-1 receptor, and ST2L/T1, an IL-1R-like molecule, is found on Th2 cells. Chemokine receptors CXCR-3 and CCR-5 are also characteristic of Th1 cells, while CXCR-4, CCR-3, CCR-4, CCR-7 and CCR-8 are associated with Th2 cells. CD30, a member of the TNF superfamily, is associated with Th2 cells. The Th1/Th2 pattern can be polarized by poxvirus administration, resulting in a phenotype that favors the secretion, etc., of cytokines that inhibit HIV infection and/or render cells resistant to infection. One or more of the aforementioned molecules can be utilized as markers of poxvirus efficacy

- Antibodies that specifically recognize HIV, e.g., neutralizing antibodies

- Antibodies that specifically recognize poxvirus

- Complement control protein. *Vaccinia* virus encodes a secreted complement control protein (VCP, 35-kDa) protein with sequence homology to the SCR-containing complement control protein superfamily. It binds C3b and C4b, and interferes with the complement cascade by providing cofactor activity for the cleavage of C3 and C4 by factor I, and by accelerating the decay of the C3 converse of both the alternative and, more effectively, the classical pathway of complement

activation. VCP may suppress the complement system or their receptor expression, rendering the host less susceptible to the complement-enhancement of HIV infection

- Activation state of a cytokine receptor, e.g., CCR5 receptor or other HIV chemokine coreceptor. For example, poxvirus can interfere with CCR5 activation
- 5 after HIV binding, e.g., by modulating tyrosine kinase feedback pathways
  - One or more of the vaccinia proteins listed in Tables 1 and 2. This includes any poxvirus-encoded protein that specifically interferes with CCR5/CD4/gp120 interactions, including, e.g., vaccinia encoded CC chemokine binding proteins and/or IFN-gamma receptor-like protein
- 10 - RNA interference with HIV expression/replication in infected cell
  - Alpha-defensins 1, 2, and/or 3
  - Soluble factors including those produced by CD8+ lymphocytes and sometimes referred to as CAF
    - Interference with the HIV life cycle, including viral entry, import into the
- 15 host cell nucleus, viral integration into host genome, Rev-dependent and Rev-independent transport from the host nucleus, replication, gene expression, RNA splicing, etc
  - Inhibiting HIV replication, including its ability to make copies of itself in the cell, and for productive viral particles to be extruded into the blood
- 20 - Inhibiting the ability of HIV to infect a cell, e.g., to bind to CD4 and/or its coreceptor, for the envelope protein to fuse with the host cell membrane, etc.
  - Modulating gene expression of the HIV virus, including modulating regulatory genes (e.g., tat and rev), accessory genes (e.g., vif, vpu, vpr, and nef), structural genes (e.g., gag, pol, and env), inner core polypeptides (e.g., gag, p17, p24, 25 p7, and p9), viral enzymes (pol, reverse transcriptase, protease, and integrase), and envelope proteins (e.g., env, gp120, and gp41). The phrase "gene expression" is used broadly to mean any step in the pathway from viral RNA to protein synthesis, and therefore includes all regulatory processes, transcription, translation, polypeptide processing, etc.
- 30 - Modulating activity of a HIV encoded polypeptide, including, tat, rev, vif, vpu, vpr, nef, gag, p17, p24, p7, p9, pol, reverse transcriptase, protease, integrase, env, gp120, gp41, etc.

- Modulating viral regulatory sequences, such as RRE, cis-acting repressive sequences (CRS), and inhibitory/instability RNA sequences (INS)
  - Any cell or tissue of the immune system, including, but not limited to, lymphocytes, B lymphocytes, T lymphocytes, helper T cells, cytotoxic (or cytolytic) T cells ("CTL), natural killer (NK) cells, naïve T cells, memory T cells, CD4+ helper T cells, CD8+ CTLs, monocytes, macrophages, antigen-presenting cells (APCs), dendritic cells, granulocytes, etc.

5 The present invention also provides kits comprising a poxvirus. For example, a kit for preventing HIV infection, comprising: an effective amount of a poxvirus, and instructions for administering an effective amount of said poxvirus to a subject to prevent HIV infection; and a kit for treating HIV infection, comprising: an effective amount of a poxvirus, and instructions for administering an effective amount of said poxvirus to a subject to treat HIV infection. The instructions can provide any information that is useful for directing the administration of the poxvirus for the 10 desired purpose.

15 The present invention also provides methods of advertising, licensing, selling, purchasing, etc., a poxvirus for the purpose of treating and/or preventing HIV infection. Methods can comprise, one or more of the following steps in any effective order: e.g., displaying information (a) comprising instructions for administering a 20 poxvirus for treating and/or preventing HIV infection or (b) comprising a description of the use of poxvirus for treating and/or preventing HIV infection, in a printed or computer-readable medium (e.g., on the Web, Internet, personal computer, server, etc); offering for sale a poxvirus for treating and/or preventing HIV infection in a printed or computer-readable medium; accepting an offer to purchase poxvirus for 25 said use in a printed or computer-readable medium.

## EXAMPLES

The following experiments were performed in the laboratory of Dr. Beda Brichacek and Dr. Michael Bukrinsky of the Department of Microbiology and Tropical Medicine, The George Washington University, Washington D.C. 20037.

5

### Methods

#### Subject selection and specimen collection.

Twenty subjects were chosen for inclusion in the study. Ten subjects had been immunized with vaccinia within the previous 3 to 6 months, and ten subjects had 10 never been immunized with vaccinia. All subjects were healthy and had a negative HIV test within the previous year. No subjects of northern European descent were used in order to avoid the potentially complicating factor of including a subject who might be homozygous for the CCR5-delta32 mutation. Two tubes of heparinized blood and 1 serum separator tube were collected. All blood samples from all subjects 15 were drawn within 6 hours of each other, and were immediately processed to separate the PBMCs using standard methods of Ficoll-Hypaque centrifugation.

#### Cell culture preparation.

PBMCs were centrifuged at 1200 rpm for 11 minutes and resuspended in 20 RPMI tissue culture medium + 10% fetal calf serum + 10 µg/ml gentamicin at a concentration of about  $1-3 \times 10^6$  cells/ml with a final concentration of  $2 \times 10^6$  cells/culture. Cell cultures were incubated in a CO<sub>2</sub> incubator. On the second day, one of the utilized strains of HIV was mixed with either culture medium or serum from each individual subject and incubated on ice for 7 hours after which 175 µl of 25 each mixture was added to the autologous cell cultures. The next day 1 ml of cell culture media was added and the cultures were incubated for 5 hours to dilute the viral inoculum and to allow the virus to detach. The supernatant was carefully aspirated and 1 ml of fresh media was added before the cultures were spun down at 1000 rpm for 7 minutes. The supernatant was again aspirated and 2 ml of fresh media was 30 added to each culture. 150 µl of supernatant for RT analysis was aspirated from each culture tube on days 2, 5, 8 and 10, and if needed, up to an additional 1 ml was aspirated and replaced with fresh media. On day 2, PHA was added to the tubes of

culture series F to act as a cell activator. On day 5, 2 ml of supernatant was removed from each of tubes of culture series F and replaced with 2 ml media + human serum + IL-2.

5 **Reverse Transcriptase (RT) analysis.**

The measurements of viral replication were performed by standard RT assays using tritiated thymidine as described in numerous articles in the scientific literature. See, e.g., Rey et al., *Virology*, 181(1), 165-71, 1991.

10 **Results**

All results are based on RT analysis using tritiated thymidine, and are given in counts per minute (CPM).

Culture Series A, the control, demonstrated no viral replication in any cultures.

15 Culture Series B (without serum; Fig. 1A) demonstrated a significant reduction of viral replication in most cultures from vaccinated subjects when compared to unvaccinated subjects. Two subjects (1 and 10) showed a complete lack of viral replication, comparable to the controls in culture series A. One subject was excluded from all analyses when it was subsequently discovered that the subject had  
20 had a highly anomalous reaction to the vaccinia immunization with recurrent skin lesions for months afterward. This suggested an inadequate immune response to the vaccinia, and this subject correspondingly did not show any protection against HIV in cell culture, demonstrating viral replication comparable to unvaccinated subjects.

Culture Series C (with serum; Fig. 1B) also demonstrated a significant  
25 reduction of viral replication in most cultures from vaccinated subjects, when compared to unvaccinated subjects. The same two subjects (1 and 10) noted in culture series B also had no demonstrable viral replication, comparable to the controls in culture series A. The addition of autologous serum in culture series C further enhanced the difference between vaccinated and unvaccinated subjects when  
30 compared to culture series B (no serum).

Culture Series D, E and F, using the T-cell (CXCR4) tropic HIV (Fig. 1C), demonstrated no difference between vaccinated and unvaccinated subjects, including

the two subjects (1 and 10) who were resistant to infection by the macrophage (CCR5) tropic HIV in culture series B and C. As stated in the methods section, care was taken in the selection of subjects to avoid those of northern European descent who might be homozygous for the CCR5-delta32 mutation, so this cannot be an 5 explanation for the described resistance. There was also no difference noted between the addition of serum and no serum (cultures D and E).

### Discussion

By at least day 10, there is a statistically significant difference between the 10 vaccinated and non-vaccinated subjects in culture series B and C ( $p=.035$  and  $.013$  respectively) that increases by day 13 ( $p=.017$  and  $.008$  respectively), indicating a resistance to infection by HIV in the vaccinated subjects (Fig. 1). Subjects 1 and 10 demonstrated total resistance to macrophage (CCR5) tropic HIV infection in both culture series B and C, with RT measurements equal to the non-HIV infected control 15 (culture series A). The fact that the same result was achieved in both sets of cultures, while infection was easily achieved with the T-cell (CXCR4) tropic HIV in cultures D, E and F, indicate these finding were not the result of laboratory error.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The 20 following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. The entire disclosure of all applications, patents and publications, cited above and in the figures are hereby incorporated by reference in their entirety, including of U.S. Provisional Application Nos. 60/491,258 filed July 31, 2003, 25 60/493,767 filed August 11, 2003, 60/496,908 filed August 22, 2003, and 60/501,832 filed September 11, 2003.

-20-

TABLE 1  
THE OPEN READING FRAMES OF VACCINIA VIRUS

Gene <sup>a</sup>	Translation Start	Stop <sup>b</sup>	Size aa	M <sub>r</sub> <sup>c</sup>	Characteristics <sup>d</sup>	References
C23L*	5008	4277	244	26.4	Nonessential; B29R Acidic <sup>e</sup> (4.2)	Perkus, et al. (1990b)
C22L*	6113	5748	122	13.6	Nonessential; B28R Hydrophobic N-terminus	Perkus, et al. (1990b)
C21L*	6815	6477	113	13.4	Nonessential; B27R	Perkus, et al. (1990b)
C20L*	7132	6824	103	12.5	Nonessential; B26R Basic (9.0)	Perkus, et al. (1990b)
C19L*	7856	7080	259	30.5	Nonessential; B25R Hydrophobic N-terminus	Perkus, et al. (1990b)
C18L*	8693	8244	150	17.5	Nonessential; B24R Acidic (4.8)	Perkus, et al. (1990b)
C17L*	9947	8790	386	44.9	Nonessential; B23R	Perkus, et al. (1990b)
C16L*	10539	9997	181	21.0	Nonessential; B22R	Perkus, et al. (1990b)
C15L*	11153	10881	91	10.5	Nonessential; B21R	Perkus, et al. (1990b)
C14L	12212	11967	82	9.3	Nonessential Basic (9.2)	Perkus, et al. (1990b)
C13L	12510	12316	65	7.4	Nonessential Acidic (4.0)	Perkus, et al. (1990b)
C12L	13733	12675	353	40.4	Serine Protease Inhibitor Nonessential Acidic (4.8)	Kotwal and Moss (1988b) Perkus, et al. (1990b)
C11R	14178	14603	142	15.8	Growth Factor  Nonessential  EGF-like type A domain Hydrophobic C-terminus	Blomquist, et al. (1984); Brown, et al. (1985); Reisner (1985) Buller, et al. (1988); Perkus, et al. (1990b)
C10L	15754	14762	331	38.5	Nonessential Acidic (4.5)	Perkus, et al. (1990b)
C9L	18136	16235	634	74.7	Nonessential	Perkus, et al. (1990b); Kotwal and Moss (1988b)
C8L	18733	18182	184	21.6	Nonessential	Kotwal and Moss (1988b); Perkus, et al. (1990b)
C7L	19257	18808	150	18.0	Acidic (4.4) Nonessential	Kotwal and Moss (1988b); Perkus, et al. (1990a,b)
C6L	19939	19487	151	17.4	Host range function Nonessential	Perkus, et al. (1990a); Kotwal and Moss (1988b); Perkus, et al. (1990b)
C5L	20680	20069	204	24.5	Acidic (4.8) Nonessential	Kotwal and Moss (1988b); Perkus, et al. (1990b)
C4L	21693	20746	316	37.2	Acidic (4.8) Nonessential	Kotwal and Moss (1988b); Perkus, et al. (1990b)
C3L	22551	21763	263	28.6	Nonessential	Kotwal and Moss (1988a,b); Perkus, et al. (1990b)
C2L	24156	22621	512	59.2	C4B binding protein homolog; virokine Nonessential	Kotwal and Moss (1988a); Kotwal and Moss (1988b); Perkus, et al. (1990b)
C1L	24900	24229	224	26.4	Hydrophobic N-terminus Nonessential Basic (9.0)	Kotwal and Moss (1988b); Perkus, et al. (1990b)

Reprinted from *Virology*, Vol. 179, S. J. Goebel, G. P. Johnson, M. E. Perkus, S. W. Davis, J. P. Winslow and E. Paoletti, "The Complete DNA Sequence of Vaccinia Virus", pgs. 247-266 (1990), with permission from Elsevier.

TABLE 1—Continued

Gene <sup>a</sup>	Translation Start	Stop <sup>b</sup>	Size aa	$M_r^c$	Characteristics	References
N1L	25240	24890	117	14.0	Nonessential Virokine Acidic (4.2)	Kotwal and Moss (1988b); Perkus, et al. (1990b) Kotwal and Moss (1988a)
N2L	25886	25362	175	20.8	Nonessential	Kotwal and Moss (1988a,b); Perkus, et al. (1990b)
M1L	27346	25931	472	54.2	Nonessential Homology to K1L	Perkus, et al. (1990b) Perkus, et al. (1990a)
M2L	27986	27327	220	25.1	Nonessential Hydrophobic N-terminus	Perkus, et al. (1990b)
K1L	28975	28124	284	32.6	Host range function Nonessential	Gillard, et al. (1986); Perkus, et al. (1989) Perkus, et al. (1990b)
K2L	30313	29207	369	42.3	Serine protease inhibitor Nonessential Basic (9.3)	Boursnell, et al. (1988) Perkus, et al. (1990b)
K3L	30629	30366	88	10.5	Nonessential Basic (9.3) Translation initiation factor	Perkus, et al. (1990b)
K4L	31955	30684	424	48.9	Homology to F13L Nonessential	Boursnell, et al. (1988) Perkus, et al. (1990b)
K5L	32497	32090	136	15.2	Nonessential Basic (10.2)	Perkus, et al. (1990b)
K6L	32764	32522	81	9.1	Nonessential	Perkus, et al. (1990b)
K7R	32903	33349	149	17.5	Nonessential Acidic (4.4) Hydrophobic C-terminus	Perkus, et al. (1990b)
F1L	34097	33420	226	26.4	Nonessential Acidic (4.4) Hydrophobic C-terminus	Perkus, et al. (1990b)
F2L	34552	34112	147	16.3	Retroviral protease Nonessential dUTPase	Slabaugh and Roseman (1989) Perkus, et al. (1990b)
F3L	36018	34579	480	55.7	Nonessential	Perkus, et al. (1990b)
F4L	36988	36032	319	37.0	Ribonucleotide reductase (small subunit) Nonessential Acidic (4.6)	Slabaugh, et al. (1988) Perkus, et al. (1990b)
F5L	37985	37023	321	36.5	Multiply hydrophobic	
F6L	38239	38018	74	8.6	Acidic (4.1)	
F7L	38533	38258	92	11.0	- (Lys-Asn),	
F8L	38878	38684	65	7.8	Basic (9.9)	
F9L	39576	38941	212	23.8	Hydrophobic C-terminus	
F10L	40882	39566	439	52.2	Protein kinase 2nd signature	
F11L	41969	40908	354	39.7	-	
F12L	43919	42015	635	73.2	-	
F13L	45079	43964	372	41.8	Envelope antigen	Hirt, et al. (1986)
F14L	45318	45100	73	8.3	Acidic (2.9)	
F15L	46068	45595	159	18.6	Basic (9.5)	
F16L	46770	46078	231	26.6	Basic (9.6)	
F17R	46833	47135	101	11.3	Basic (9.8)	
E1L	48574	47138	479	55.6	-	
E2L	50784	48574	737	85.9	-	
E3L	51483	50914	190	21.5	Acidic (4.9)	
E4L	52318	51542	259	29.8	Acidic (4.9) Transcription factor	

TABLE 1—Continued

Gene <sup>a</sup>	Translation Start	Stop <sup>b</sup>	Size aa	M <sub>r</sub> <sup>c</sup>	Characteristics	References
E5R	52395	53387	331	39.1	(ts: C19??) <sup>f</sup> Basic (9.8)	Condit, et al. (1983)
E6R	53527	55227	567	66.7	—	
E7R	55314	55811	166	19.5	—	
E8R	55939	56757	273	31.9	Basic (9.3)	
E9L	59787	56770	1006	117.0	DNA Polymerase ts: C42, NG26; PAA <sup>f</sup> , Aphidicolin <sup>f</sup> DNA polymerase family B signature	Earl, et al., 1986 Traktman, et al. (1989b)
E10R	59819	60103	95	10.8	—	
E11L	60490	60104	129	14.9	—	
O1L	62477	60480	656	77.6	Leucine Zipper Motif	
O2L	62851	62528	108	12.4	Glutaredoxin	
I1L	63935	63000	312	35.8	—	
I2L	64163	63945	73	8.4	Hydrophobic C-terminus Acidic (3.9)	
I3L	64973	64167	269	30.0	—	
I4L	67371	65059	771	87.0	Ribonucleotide reductase (large subunit) Nonessential	Schmitt and Stunnenberg (1988) Tengelsen, et al. (1988) Perkus, et al. (unpublished) Child, et al., (1990)
I5L	67637	67401	79	8.7	Divalent Fe-S ferredoxin binding region signature	
I6L	68804	67659	382	43.4	Basic (9.9)	
I7L	70068	68800	423	49.0	Basic (9.2)	
I8R	70074	72101	676	77.6	ATP/GTP binding motif A	
G1L	73883	72111	591	67.9	—	
G2R	74209	74868	220	25.7	—	
G3L	74215	73883	111	12.8	Hydrophobic N-terminus	
G4L	75215	74844	124	14.0	Acidic (4.8)	
G5R	75218	76519	434	49.9	Acidic (4.8)	
G6R	76723	77217	165	18.9	—	
G7L	78300	77188	371	41.9	—	
G8R	78331	79110	260	29.9	—	
G9R	79133	80152	340	38.8	Hydrophobic C-terminus	
L1R	80156	80905	250	27.3	Hydrophobic near C-terminus	
L2R	80940	81200	87	10.2	—	
L3L	82245	81196	350	40.6	Multiply hydrophobic	
L4R	82270	83022	251	28.5	Structural protein, VP8	Yang, et al. (1988)
L5R	83035	83418	128	14.0	Basic (10.0)	
J1R	83378	83836	153	17.8	—	
J2R	83855	84385	177	20.1	Thymidine kinase Nonessential ATP/GTP binding motif A	Weir and Moss (1983); Hruby et al. (1983) Mackett, et al. (1982)
J3R	84454	85452	333	15.2	Basic (10.0)	
J4R	85370	85924	185	21.3	RNA Polymerase subunit ts: C7, C20	Broyles and Moss (1986) Hooda-Dhingra, et al. (1989); Thompson, et al. (1989)
J5L	86403	86005	133	15.2	Hydrophobic C-terminus	
J6R	86510	90367	1286	146.8	RNA Polymerase subunit ts: E8, E13, E72 C51, C53, C65	Broyles and Moss (1986) Ensinger (1987) Hooda-Dhingra, et al., (1989); Thompson, et

TABLE 1—Continued

Gene <sup>a</sup>	Translation Start	Stop <sup>b</sup>	Size aa	M <sub>r</sub> <sup>c</sup>	Characteristics	References
H1L	90882	90370	171	19.7	Basic (9.6)	
H2R	90896	91462	189	21.5	Hydrophobic N-terminus	
H3L	92442	91471	324	37.5	Multiply hydrophobic	
H4L	94830	92446	795	93.6	-	
H5R	95016	95624	203	22.3	-	
H6R	95628	96569	314	36.7	Basic (10.0) DNA topoisomerase	
H7R	96609	97046	146	16.9	-	Shuman and Moss (1987)
D1R	97093	99624	844	96.7	mRNA capping enzyme (small subunit)	Morgan, et al. (1984)
D2L	100026	99589	146	16.9	ts: E52, E94	Seto, et al. (1987)
D3R	100019	100729	237	28.0	ts: C5, C35	Seto, et al. (1987)
D4R	100732	101385	218	25.0	-	Seto, et al. (1987)
D5R	101420	103774	785	90.0	ts: C17, C24, E69 ATP/GTP binding motif A	Broyles and Fesler (1990)
D6R	103818	105728	637	73.8	Early transcription factor subunit ts: C46, E93 Hydrophobic N-terminus	Seto, et al. (1987)
D7R	105758	106240	161	17.9	RNA polymerase subunit ts: C21, E45 Acidic (4.5)	Ahn, et al. (1990) Seto, et al. (1987)
D8L	107120	106209	304	35.3	Carbonic anhydrase Transmembrane Cell surface binding Multiply hydrophobic Basic (9.1)	Niles, et al. (1986) Niles and Seto (1988) Maa, et al (1990)
D9R	107162	107800	213	25.0	-	
D10R	107800	108543	248	28.9	-	
D11L	110442	108550	631	72.4	NTPase	Rodriguez, et al. (1986); Broyles and Moss (1987) Seto, et al. (1987)
D12L	111340	110480	287	33.4	ts: C36, C50, E17 Basic (9.0) mRNA capping enzyme (small subunit)	Niles, et al. (1989)
D13L	113026	111374	551	61.9	ts: C33, C43, E101 Rifampicin resistance Acidic (5.0)	Seto, et al. (1987) Tartaglia and Paoletti (1985); Baldick and Moss (1987)
A1L	113502	113053	150	17.0	-	Rosel and Moss (1985)
A2L	114197	113526	224	26.3	-	
A3L	116372	114441	644	72.6	Major core protein P4b	
A4L	117270	116428	281	30.8	Acidic (4.6)	
A5R	117308	117799	164	19.0	Acidic (4.2)	
A6L	118917	117802	372	43.1	-	
A7L	121073	118944	710	82.3	Early transcription factor subunit	Gershon and Moss (1990)
A8R	121127	121990	288	33.6	-	
A9L	122285	121989	99	11.1	-	
A10L	124961	122289	891	102.3	Major core protein P4a	Van Meir and Wittek (1988)
A11R	124976	125929	318	36.1	Hydrophobic C-terminus Acidic (4.7)	
A12L	126512	125937	192	20.5	Basic (10.1)	
A13L	126748	126539	70	7.7	Basic (9.7)	
A14L	127128	126859	90	10.0	-	
A15L	127580	127299	94	11.0	-	
A16L	128700	127567	378	43.6	Hydrophobic C-terminus	
A17L	129314	128706	203	23.0	Hydrophobic center Acidic (4.1)	
A18R	129329	130807	493	56.7	Basic (9.3)	

TABLE 1—Continued

Gene <sup>a</sup>	Translation Start	Stop <sup>b</sup>	Size aa	M <sub>r</sub> <sup>c</sup>	Characteristics	References
A19L	131024	130794	77	8.3	—	
A20R	131377	132654	426	49.2	—	
A21L	131378	131028	117	13.6	Hydrophobic N-terminus	
A22R	132620	133147	176	20.7	Basic (9.9)	
A23R	133170	134315	382	44.6	—	
A24R	134315	137806	1164	133.4	RNA polymerase subunit; ts: C27, C29, C32, C47, C62	Hooda-Dhingra, et al. (1990)
A25L	138011	137817	65	7.5	Leucine Zipper Pattern A-type inclusion protein (cowpox virus)	Hooda-Dhingra, et al. (1990)
A26L	138948	137983	322	37.3	Acidic (3.3) A-type Inclusion protein (cowpox virus)	Funahashi, et al. (1988);
A27L	139330	139001	110	12.6	Basic (9.2) Fusion protein	Rodriguez & Esteban (1987)
A28L	139771	139334	146	16.3	—	
A29L	140689	139775	305	35.4	—	
A30L	140885	140655	77	8.7	Basic (9.9)	
A31R	141045	141416	124	14.2	Basic (9.0)	
A32L	142288	141389	300	34.4	Ribonucleoprotein RNA-binding region signature Basic (9.2) ATP/GTP Binding motif A	
A33R	142316	142870	185	20.5	—	
A34R	142897	143400	168	19.5	Basic (10.1)	
A35R	143447	143974	176	20.0	Acidic (4.0)	
A36R	144044	144706	221	25.1	Acidic (4.4)	
A37R	144773	145561	263	29.9	—	
A38L	146678	145848	277	31.6	Multiply hydrophobic	
A39R	146695	147903	403	45.7	—	
A40R	147932	148435	168	19.3	Hydrophobic N-terminus	
A41L	149155	148499	219	25.1	Acidic (4.8)	
A42R	149334	149732	133	15.0	Basic (9.9) Profilin	
A43R	149773	150354	194	22.6	—	
A44L	151733	150696	346	39.4	3 $\beta$ -Hydroxy-5-ene steroid dehydrogenase	
A45R	151780	152154	125	13.8	Superoxide dismutase	
A46R	152147	152788	214	24.7	—	
A47L	153690	152959	244	28.3	Basic (10.0)	
A48R	153789	154400	204	23.2	Thymidylate kinase ATP/GTP binding motif A	Smith, et al. (1989a)
A49R	154451	154936	162	18.8	Acidic (5.0)	
A50R	154972	156627	552	63.4	Acidic (3.9) DNA Ligase	Colinas, et al. (1990); Smith, et al. (1989a); Kerr and Smith (1989)
A51R	156683	157684	334	37.7	Nonessential	Colinas, et al. (1990)
A52R	157757	158326	190	22.7	Nonessential	Davis, et al. (unpublished)
A53R	158635	158943	103	12.0	Hydrophilic N-terminus	Davis, et al. (unpublished)
A54L	158743	158474	90	10.8	Nonessential	Davis, et al. (unpublished)
A55R	159442	161133	564	64.7	Basic (10.4)	Davis, et al. (unpublished)
A56R	161186	162130	315	34.8	Nonessential	Davis, et al. (unpublished)
					Hemagglutinin	Shida, et al. (1987)
					Hydrophobic C-terminus	Shida (1986)
A57R	162278	162730	151	17.4	Acidic (3.9)	
					—	

TABLE 1—Continued

Gene <sup>a</sup>	Translation Start	Stop <sup>b</sup>	Size aa	$M_r^c$	Characteristics	References
B1R	162884	163783	300	34.3	ts: C2, C3, C25 Protein Kinase Basic (9.1)	Traktman, et al. (1989a) Howard and Smith (1989)
B2R	163876	164532	219	24.6	—	
B3R	164571	164942	124	14.4	Acidic (4.7)	
B4R	165603	167276	558	65.3	—	
B5R	167383	168333	317	35.1	Multiply hydrophobic Acidic (4.4) Complement control proteins C3L homologue	
B6R	168432	168950	173	20.1	—	
B7R	168991	169536	182	21.3	Hydrophobic N-terminus	
B8R	169594	170409	272	31.2	Hydrophobic N-terminus	
B9R	170499	170729	77	8.8	—	
B10R	170695	171192	166	18.9	—	
B11R	171267	171530	88	9.9	Acidic (3.6) M(DT) <sub>6</sub> DVTNV...	
B12R	171600	172448	283	33.4	Protein Kinase	Howard and Smith (1989)
B13R	172562	172909	116	12.8	Hemorrhage-inducing Serine Protease Inhibitor Nonessential Acidic (4.6)	Pickup, et al. (1986) Kotwal and Moss (1989); Perkus, et al. (1990b)
B14R	172887	173552	222	24.9	Hemorrhage-inducing Serine Protease Inhibitor Nonessential Acidic (4.3)	Pickup, et al. (1986) Kotwal and Moss (1989) Perkus, et al. (1990b)
B15R	173632	174078	149	17.4	Nonessential Acidic (4.5)	Perkus, et al. (1990b)
B16R	174272	175141	290	32.5	Nonessential Kinase-related transforming protein	Perkus, et al. (1990b)
B17L	176212	175193	340	39.5	Nonessential	Perkus, et al. (1990b)
B18R	176349	178070	574	68.1	Nonessential	Perkus, et al. (1990b)
B19R	178145	179203	353	40.9	Hydrophobic N-terminus	
B20R	179300	179680	127	15.5	Nonessential Nonessential Acidic (4.1)	Perkus, et al. (1990b) Perkus, et al. (1990b)
B21R*	180585	180857	91	10.5	Nonessential; C15L	Perkus, et al. (1990b)
B22R*	181199	181741	181	21.0	Nonessential; C16L	Perkus, et al. (1990b)
B23R*	181791	182948	386	44.9	Nonessential; C17L	Perkus, et al. (1990b)
B24R*	183045	183494	150	17.5	Nonessential; C18L Acidic (4.8)	Perkus, et al. (1990b)
B25R*	183882	184658	259	30.5	Hydrophobic N-terminus	
B26R*	184606	184914	103	12.5	Nonessential; C19L Nonessential; C20L Basic (9.0)	Perkus, et al. (1990b) Perkus, et al. (1990b)
B27R*	184923	185261	113	13.4	Nonessential; C21L	Perkus, et al. (1990b)
B28R*	185625	185990	122	13.6	Nonessential; C22L Hydrophobic N-terminus	Perkus, et al. (1990b)
B29R*	186730	187461	244	26.4	Nonessential; C23L Acidic (4.2)	Perkus, et al. (1990b)

<sup>a</sup> Open reading frames enumerated as described in text.<sup>b</sup> Translation stop does not include the three bases of termination codon.<sup>c</sup>  $M_r$  values calculated for the nascent, unprocessed polypeptide chain are presented as kDa.<sup>d</sup> Functions or activities indicated in bold type are known functions of vaccinia virus. Those indicated in *italics* have been identified in this study on the basis of similarity to existing proteins. All others are possible functions previously described by other investigators.<sup>e</sup> Acidic proteins: pI < 5.0; basic proteins: pI > 9.0. pI presented within parentheses.<sup>f</sup> Temperature-sensitive mutants indicated by *ts*. Those first isolated by Condit et al. (1983) are prefaced with C; 1 begin with E. Mutant C19, while not localized to a particular open reading frame, appears to map in the vicinity of I.<sup>g</sup> Open reading frames repeated in both left and right termini of genome.

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TABLE 2  
Features and Homologies of Open Reading Frames of the Vaccinia MVA Strain

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA Id	HSS <sup>f</sup> (%)	references
	STOP			left terminal region:				
001L/193R <sup>b</sup>	6822	136	14.9	35k major secr. protein chemokine receptor (f1) VAC (C23L/B29R)	6.0e-57	41/42	97	(Patel <i>et al.</i> , 1990) (Graham <i>et al.</i> , 1997)
<i>C23L</i>		244		VAR-1 <sup>b</sup> G3R	8.9e-51	46/49	93	(Goebel <i>et al.</i> , 1990)
		253		CPX ORFB	5.6e-49	40/42	95	(Shchelkunov <i>et al.</i> , 1995)
		246		SFV T1 protein	2.5e-20	23/42	54	(Hu <i>et al.</i> , 1994)
		258		Myxoma virus T1/35kDa	1.5e-14	21/42	50	(Upton <i>et al.</i> , 1987) (Graham <i>et al.</i> , 1997)
		260						
002L/192R <sup>b</sup>	7784	176	19.7	secr. TNF receptor (f1) CPX crmB	5.1e-71	76/83	91	(Upton <i>et al.</i> , 1991a) (Hu <i>et al.</i> , 1994)
	7254	355		VAR-BSH G2R	1.0e-66	73/83	87	(Shchelkunov <i>et al.</i> , 1995)
		348		Myxoma virus T2	4.9e-30	21/37	56	(Upton <i>et al.</i> , 1991a)
		326		Rabbit fibroma Virus T2	1.8e-28	17/36	47	(Upton <i>et al.</i> , 1987)
		325		CPX C4L	8.7e-13	30/51	58	(Safronov <i>et al.</i> , 1996)
<i>C19L</i>		202		'HS TNF receptor protein	1.9e-08	14/26	53	(Heller <i>et al.</i> , 1990)
		346		VAC (C19L/B25R)	0.00026	16/19	84	(Goebel <i>et al.</i> , 1990)
		259		human CD40L receptor	0.0015	11/24	45	(Stamencovic <i>et al.</i> , 1989)
		277		30 matches to TNF receptors and surface proteins	<0.39			
003L/191R <sup>b</sup>	8780	102	12.1	45k ank-like protein (f1)				(Goebel <i>et al.</i> , 1990)
<i>C17L</i>	8472			VAC C17L/B23R	1.3e-39	62/63	98	(Goebel <i>et al.</i> , 1990)
004L/190R <sup>b</sup>	9558	233	26.9	45k ank-like protein (f2)				(Goebel <i>et al.</i> , 1990)
<i>C17L</i>		386		VAC (C17L/B23R)	6.2e-159	110/110	100	(Goebel <i>et al.</i> , 1990)
<i>D1L</i>		91		VAR-BSH	9.1e-31	46/49	93	(Shchelkunov <i>et al.</i> , 1995)
		669		CPX host range	1.1e-13	22/50	44	(Spehner <i>et al.</i> , 1988)
		452		VAR-1 D6L (BSH:D8L)	1.7e-11	21/50	42	(Shchelkunov <i>et al.</i> , 1995)
		574		VAR-1 B19R (BSH: B16R)	1.2e-05	22/73	30	(Shchelkunov <i>et al.</i> , 1995)
		574		VAC B18R (WR: B17R)	8.6e-05	22/73	30	(Goebel <i>et al.</i> , 1990)
		634		VAC C9L	0.00011	11/24	45	(Kotwal and Moss, 1988a)
		585		VAR-1 GIR	0.00013	22/74	29	(Shchelkunov <i>et al.</i> , 1995)
		516		orf virus	0.0088	15/49	30	(Sullivan <i>et al.</i> , 1995b)
		153		VAR-1 D7L (BSH:D10L)	0.014	12/28	42	(Shchelkunov <i>et al.</i> , 1995)
005R	10203	140	15.5	Growth factor (EGF receptor binding)				(Twardzik <i>et al.</i> , 1985)
<i>C11R</i>	10625			VAC	2.9e-82	99/104	95	(Stroobant <i>et al.</i> , 1985)
<i>D2R</i>		142		VAR-1 (BSH:D4R)	3.6e-74	106/140	75	(Goebel <i>et al.</i> , 1990)
		140		CPX D5R	3.4e-95	101/114	88	(Shchelkunov <i>et al.</i> , 1995)
		138		human epiregulin	2.2e-14	29/78	37	(Safronov <i>et al.</i> , 1996)
		169		100 matches to growth factor like sequences	<0.10			D30783
006L	11758	326	37.9	37.9k protein				(Venkatesan <i>et al.</i> , 1982)
<i>C10L</i>	10778	331		VAC	1.7e-235	264/268	98	(Goebel <i>et al.</i> , 1990)
		331		CPX D6L	7.7e-235	264/268	98	(Safronov <i>et al.</i> , 1996)
<i>D5L</i>		330		VAR-BSH (I: D3L)	3.6e-233	169/171	97	(Shchelkunov <i>et al.</i> , 1995)
		316		VAR-1 D11L (BSH:D14L)	1.7e-94	34/68	44	(Shchelkunov <i>et al.</i> , 1995)
		316		VAC C4L	1.8e-92	30/68	54	(Goebel <i>et al.</i> , 1990)
		315		CPX D16L	2.3e-92	31/68	45	(Safronov <i>et al.</i> , 1996)
		82		Ectromelia 42k protein	1.2e-50	78/82	95	(Senkevich <i>et al.</i> , 1993a)
		418		FPV BamHI ORF1	3.0e-11	13/41	31	(Tomley <i>et al.</i> , 1988)
007R	12263	91	10.6	28k virulence factor (f1)				(Senkevich <i>et al.</i> , 1993a)
<i>D4R</i>	12538	242		CPX D7R	1.5e-51	42/47	89	(Safronov <i>et al.</i> , 1996)
		184		VAC-WR 21.7k protein	5.3e-51	41/47	87	(Kotwal and Moss, 1988a)
		242		VAR-1 (BSH:D6R)	3.7e-50	41/47	87	(Shchelkunov <i>et al.</i> , 1995)
		241		Ectromelia 28k secreted virulence factor	3.7e-50	41/47	87	(Senkevich <i>et al.</i> , 1993a)
008L	13414	120	13.7	13.7k protein				
<i>D7L</i>	13052	126		VAR-BSH (I:DSL)	1.9e-83	57/64	89	(Shchelkunov <i>et al.</i> , 1995)
		138		Ectromelia 16k protein	7.8e-81	58/60	96	(Senkevich <i>et al.</i> , 1993a)
		124		CPX D8L	3.2e-67	49/60	81	(Safronov <i>et al.</i> , 1996)
		68		7.8k protein (VAC-WR)	1.3e-34	53/64	82	(Kotwal and Moss, 1988a)
009L	13745	90	10.7	77k CPX hr protein (f1)				(Spehner <i>et al.</i> , 1988)
	13473	669		CPX host range gene	2.7e-46	43/52	82	(Safronov <i>et al.</i> , 1996)
		634		VACC9L	1.7e-05	9/33	27	(Goebel <i>et al.</i> , 1990)
<i>010L</i>	14186	142	16.1	77k CPX hr protein (f2)				(Spehner <i>et al.</i> , 1988)
	13758	669		CPX host range gene	2.2e-91	133/142	93	(Safronov <i>et al.</i> , 1996)
		634		VAC C9L	9.2e-21	26/63	41	(Goebel <i>et al.</i> , 1990)
<i>D6L</i>		452		VAR-1 (BSH: D8L)	4.5e-13	27/29	93	(Shchelkunov <i>et al.</i> , 1995)
		150		VAC C18L/B24R	1.3e-11	19/52	36	(Goebel <i>et al.</i> , 1990)
		439		AT ankyrin repeat protein	9.5e-07	23/59	38	(Zhang <i>et al.</i> , 1992)
		558		VAR-1 B6R (BSH:B5R)	4.0e-05	28/113	24	(Shchelkunov <i>et al.</i> , 1995)
				30 matches with ankyrin repeat containing proteins	2.7e-05 to 0.016			
011L	14682	135	15.8	77k CPX hr protein (f3)				(Spehner <i>et al.</i> , 1988)
<i>D6L</i>	14275	669		CPX host range gene	7.6e-80	54/64	84	(Safronov <i>et al.</i> , 1996)
<i>012L</i>	15183	452		VAR-1 (BSH: D8L)	9.2e-78	52/64	81	(Shchelkunov <i>et al.</i> , 1995)
		90	10.3	77k CPX hr protein (f4)				(Spehner <i>et al.</i> , 1988)

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## GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START STOP	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologues <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
<b>left terminal region:</b>								
D6L	14911	452		VAR-I (BSH: D8L)	2.2e-52	80/85	94	(Shchelkunov <i>et al.</i> , 1995)
		669		CPX host range gene	8.1e-51	77/85	90	(Spehner <i>et al.</i> , 1988)
		153		VAR-I D7L (BSH: D10L)	2.9e-17	19/45	42	(Shchelkunov <i>et al.</i> , 1995)
		634		VACC9L	1.3e-13	19/45	42	(Goebel <i>et al.</i> , 1990)
		116		C. botulinum NTN1 protein	0.00019	6/12	50	(Hutson <i>et al.</i> , 1996)
		202		Capripox	0.00058	15/58	25	(Cao <i>et al.</i> , 1995)
		895		UDP glucose dehydrogenase	0.00051	6/19	31	(Bult <i>et al.</i> , 1996)
		516		orf virus ank-like	0.0064	16/49	32	(Sullivan <i>et al.</i> , 1995b)
		673		rabbit fibroma 77.2k protein	0.0072	12/30	40	(Massung <i>et al.</i> , 1992)
013L	15420	71	8.5	77k CPX hr protein (f5)				
	15205	669		CPX host range gene	5.2e-44	68/69	98	(Spehner <i>et al.</i> , 1988)
D6L		452		VAR (BSH: D8L)	7.9e-42	64/67	95	(Shchelkunov <i>et al.</i> , 1995)
		673		rabbit fibroma 77.2k protein	0.0052	8/26	30	(Massung <i>et al.</i> , 1992)
		386		VAC C17L/B23R	0.018	14/33	42	(Goebel <i>et al.</i> , 1990)
		202		Capripox	0.023	10/19	52	(Sullivan <i>et al.</i> , 1995b)
		574		VAC B18R (WR: B17R)	0.71	12/28	42	(Goebel <i>et al.</i> , 1990)
		574		VAR B19R (BSH: B16R)	0.71	12/28	42	(Shchelkunov <i>et al.</i> , 1995)
014L	16205	109		75k ank-like gene (f1)				
C9L	15876	634		VAC	3.9e-73	109/109	100	(Kotwal and Moss, 1988a)
		614		CPX D11L	1.6e-70	105/108	97	(Goebel <i>et al.</i> , 1990)
D9L		91		VAR (I: D6.5L)	1.2e-52	78/91	85	(Safronov <i>et al.</i> , 1996)
		437		CPX D11L	3.7e-19	28/67	41	(Shchelkunov <i>et al.</i> , 1995)
015L	16786	96	11.2	rabbit fibroma 77.2K protein	0.021	5/16	31	(Safronov <i>et al.</i> , 1996)
C9L	16496	634		75k ank-like gene (f2)				(Massung <i>et al.</i> , 1992)
		614		VAC	4.0e-53	80/80	100	(Kotwal and Moss, 1988a)
		437		CPX D11L	3.9e-25	48/80	60	(Goebel <i>et al.</i> , 1990)
		172		CPX D11L	9.6e-12	14/36	38	(Safronov <i>et al.</i> , 1996)
		141		VAR-Garcia 1966 B11L	0.0001	17/17	100	(Massung <i>et al.</i> , 1996)
		669		integrase (simian foamy v.)	0.033	10/24	41	(Schweizer and Neumann, 1995)
016L	17759	297	35.0	CPX host range gene	0.043	9/17	52	(Goebel <i>et al.</i> , 1988)
C9L	16866	634		75k ank-like gene (f3)				(Kotwal and Moss, 1988a)
		614		VAC	3.4e-208	291/294	98	(Goebel <i>et al.</i> , 1990)
D7L		153		CPX D11L	1.4e-130	90/126	71	(Safronov <i>et al.</i> , 1996)
		669		VAR-I (BSH: D10L)	8.4e-68	84/109	77	(Shchelkunov <i>et al.</i> , 1995)
D8L		452		CPX host range gene	4.5e-17	24/61	39	(Spehner <i>et al.</i> , 1988)
		668		CPX D9L	2.2e-16	23/61	37	(Safronov <i>et al.</i> , 1996)
		386		VAR-BSH (I: D6L)	3.3e-16	21/61	34	(Shchelkunov <i>et al.</i> , 1995)
		833		VAC C17L/B23R	2.9e-08	11/24	45	(Goebel <i>et al.</i> , 1990)
		574		CPX D3L	0.0085	13/58	22	(Safronov <i>et al.</i> , 1996)
		202		VAC B18R (WR: B17R)	0.012	13/40	32	(Goebel <i>et al.</i> , 1990)
		574		Capripox virus	0.084	11/29	37	(Sullivan <i>et al.</i> , 1995b)
				VAR-I B19R (BSH: B16R)	0.090	13/40	32	(Shchelkunov <i>et al.</i> , 1995)
017L	18335	177	20.8	20.8k protein				
C8L	17802	184		VAC	1.2e-125	125/129	96	(Kotwal and Moss, 1988a)
		182		CPX D12L	5.0e-118	119/126	94	(Goebel <i>et al.</i> , 1990)
		182		VAC B7R	8.3e-06	16/67	23	(Safronov <i>et al.</i> , 1996)
		795		VAC H4L (RAP94)	0.60	12/45	26	(Goebel <i>et al.</i> , 1990)
018L	18859	150	18.0	host range protein				
C7L	18407	150		VAC	1.6e-106	150/150	100	(Perkus <i>et al.</i> , 1991)
D11L		150		VAR-BSH (I: D8L)	4.2e-106	149/150	99	(Kotwal and Moss, 1988a)
		185		Swinepox virus ORF SwF8a	3.4e-35	31/82	37	(Shchelkunov <i>et al.</i> , 1995)
		197		Capripox virus ORF CF8a	1.4e-31	29/87	33	(Schnitzlein and Tripathy, 1991)
		170		CPX D4L	3.5e-17	19/60	31	(Gershon and Black, 1989a)
		158		CPX D4L	3.5e-17	19/60	31	(Safronov <i>et al.</i> , 1996)
		128		Myxoma virus ORF MF8	5.6e-13	16/43	37	(Jackson and Bults, 1992)
				VAR-BSH D3L (I: D1.5L)	5.4e-06	18/60	30	(Shchelkunov <i>et al.</i> , 1995)
019L	19541	157	18.2	18.2k protein				
C6L	19068	151		VAC	7.6e-104	151/151	100	(Kotwal and Moss, 1988a)
D9L		156		VAR (BSH: D12L)	1.6e-99	145/150	96	(Goebel <i>et al.</i> , 1990)
		156		CPX D14L	1.3e-96	141/150	94	(Shchelkunov <i>et al.</i> , 1995)
		159		Capripox virus ORF T3a	4.4e-07	24/76	31	(Safronov <i>et al.</i> , 1996)
		151		Rabbit fibroma virus T3Aa	0.0047	16/46	34	(Gershon and Black, 1989a)
		181		VAC C16L/B22R	0.2	12/46	26	(Upton <i>et al.</i> , 1987)
		149		VAR C4R	0.29	8/13	61	(Goebel <i>et al.</i> , 1990)
		149		VAC-WR K7R	0.40	8/13	61	(Shchelkunov <i>et al.</i> , 1995)
								(Kotwal and Moss, 1988a)
020L	20025	113	13.2	14k virulence factor, secreted protein (f)				
N1L	19684			VAC	2.6e-60	92/102	90	(Kotwal and Moss, 1988b)
P1L		117		CPX PIL	7.3e-58	85/102	83	(Goebel <i>et al.</i> , 1990)
		117		VAR-BSH, virokine	6.6e-56	88/102	86	(Shchelkunov <i>et al.</i> , 1995)
		107		Rabbit fibroma virus	0.015	10/17	58	(Safronov <i>et al.</i> , 1996)
								(Massung <i>et al.</i> , 1992)
021L	20656	170	20.3	alpha-amanitin sensitive protein				
N2L	20144			CPX P2L	3.0e-118	138/142	97	(Tamin <i>et al.</i> , 1991)
P2L		175		VAC	6.1e-118	137/142	96	(Kotwal and Moss, 1988a)
		177		VAR	9.7e-115	135/142	95	(Safronov <i>et al.</i> , 1996)
								(Goebel <i>et al.</i> , 1990)
022L	20981	98	11.0	33k host range gene (f)				
K1L	20685	284		VAC	1.8e-56	86/88	97	(Shchelkunov <i>et al.</i> , 1995)
		284		CPX MIL	2.3e-56	86/88	97	(Gillard <i>et al.</i> , 1986)
C1L		66		VAR	2.0e-39	63/66	95	(Altenburger <i>et al.</i> , 1989)
		65		human NOTCH 2	0.00036	17/41	41	(Safronov <i>et al.</i> , 1996)

ORF <sup>a</sup>	START STOP	AA <sup>b</sup>	kDa <sup>c</sup>	name / function / (putative) homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
left terminal	region:							
023L	22296 21187	369	42.3	serpin SPI-3, cell-cell fusion mutation				(Boursnell <i>et al.</i> , 1988) (Altenburger <i>et al.</i> , 1989)
K2L		369		VAC	1.2e-258	365/369	98	(Goebel <i>et al.</i> , 1990)
C2L		373		CPX M2L	1.2e-256	331/337	96	(Safronov <i>et al.</i> , 1996)
		373		VAR-BSH	9.9e-249	321/337	95	(Shchelkunov <i>et al.</i> , 1995)
		373		Ectromelia virus H14-B	6.5e-244	312/337	95	U67964
		386		HS plasminogen activator inhibitor 1	1.1e-35	30/68	44	(Loskutoff <i>et al.</i> , 1987)
		58		CPX SPI 3 protein	8.2e-33	57/58	98	gi:1168082
		369		Myxoma virus MAPI gene	7.3e-32	33/131	25	(Upton <i>et al.</i> , 1990a)
		397		mouse protease nexin	1.5e-29	31/67	46	(Vassalli <i>et al.</i> , 1993)
		397		humane glia derived neurite-promoting factor	8.7e-27	30/65	46	A03911
		320		Swinepox SPI like protein	3.6e-21	20/70	28	(Massung <i>et al.</i> , 1993)
		417		a-1 antitrypsin, human	2.2e-20	26/66	39	(Ciliberto <i>et al.</i> , 1985)
		383		Corticosteroid-binding protein (rabbit)	9.0e-20			(Seralini <i>et al.</i> , 1989)
		390		squamous cell carcinoma antigen	1.9e-17			(Schneider <i>et al.</i> , 1995)
024L	22612 22346	88	10.5	IFN resistance, eIF-2 $\alpha$ homolog				(Beattie <i>et al.</i> , 1991) (Davies <i>et al.</i> , 1992)
K3L		88		CPX M3L	2.6e-61	88/88	100	(Safronov <i>et al.</i> , 1996)
C3L		88		VAC	1.4e-60	87/88	98	(Goebel <i>et al.</i> , 1990)
		88		VAR-I	1.0e-52	73/88	82	(Shchelkunov <i>et al.</i> , 1995)
		86		SPV C8 protein	4.1e-22	20/44	45	(Massung <i>et al.</i> , 1993)
				translation initiation factor 2 family	1.2e-08/ 0.45			
025L	23938 22664	424	48.9	phospholipase D-like protein				(Cao <i>et al.</i> , 1997)
K4L		424		VAC	1.5e-306	423/424	99	(Goebel <i>et al.</i> , 1990)
		424		CPX M4L	2.1e-303	416/424	98	(Safronov <i>et al.</i> , 1996)
		437		human HU-K4	2.8e-135	53/95	55	U60644
		372		D. discoideum	2.5e-91	28/47	59	(Giorda <i>et al.</i> , 1989)
		516		C. elegans	6.6e-89	31/61	50	gi: 2435624
		2327		C. elegans	2.8e-52	36/60	60	gi: 2291241
		635		C. elegans	1.1e-24	19/53	35	(Wilson <i>et al.</i> , 1994)
		377		FPV major envelope protein	2.9e-23	19/61	31	(Calvert <i>et al.</i> , 1992)
		371		Myxoma virus env protein	3.6e-22	18/51	35	U43549
		378		Orf virus env protein B2L	1.2e-21	21/71	29	(Sullivan <i>et al.</i> , 1994)
MC021L		388		MCV subtype I env protein	3.2e-21	20/63	31	(Senkevich <i>et al.</i> , 1997)
CI7L		372		VAR-BSH	4.6e-19	15/52	28	(Shchelkunov <i>et al.</i> , 1995)
		372		VAC F13L	4.9e-17	15/52	28	(Goebel <i>et al.</i> , 1990)
026L	24478 23966	170	19.1	lysophospholipase-like protein (f1)				(Upton & Buller, unpub.)
K5L		276		CPX M5L	2.6e-110	161/170	94	(Safronov <i>et al.</i> , 1996)
		277		Ectromelia virus H14-E	2.7e-109	160/170	94	X94355 U67964
		136		VAC	5.5e-69	107/108	99	(Goebel <i>et al.</i> , 1990)
		134		VAC-WR	8.3e-63	98/101	97	(Boursnell <i>et al.</i> , 1988)
		313		HS lysophospholipase homolog	3.3e-35	35/105	33	U67963
		323		poss. oxidoreductase M. tuberculosis	1.2e-13	30/94	31	Z97050
		324		Lysophospholipase isolog	3.1e-5	13/58	22	U95973
		313		A. thaliana	0.047	13/30	43	U32747
				H. influenza probable				
027L	24694 24500	64	7.0	lysophospholipase L2				(Upton & Buller, unpub.)
K6L		81		lysophospholipase-like protein (f2)				
		276		VAC	5.3e-42	63/63	100	(Boursnell <i>et al.</i> , 1988)
		277		CPX MSL	2.4e-36	57/58	98	(Safronov <i>et al.</i> , 1996)
		313		Ectromelia virus H14-E	2.4e-36	57/58	98	U67964
		323		HS lyophospholipase homolog	9.1e-23	34/53	64	U67963
				hyp. oxidoreductase M. tuberculosis	9.9e-14	22/54	40	Z97050
		530		dihydrotestosterone/androsta-nediol UDP-glucuronosyl-transferase	7.0e-05	6/17	35	A48633
central conserved	region:							
028R	24864	149	17.5	17.5k protein				
K7R	25313	149		VAC	6.1e-105	149/149	100	(Goebel <i>et al.</i> , 1990)
		161		CPX M6R	1.6e-101	144/149	96	(Goebel <i>et al.</i> , 1990)
C4R		149		VAR	4.9e-101	143/149	100	(Safronov <i>et al.</i> , 1996)
		236		Swinepox (sc76)	0.00017	19/49	95	(Shchelkunov <i>et al.</i> , 1995)
				(Massung <i>et al.</i> , 1993)				
029L	26046	222	25.9	25.9k protein				
F1L	25378	226		VAC	2.7e-158	208/211	98	(Roseman and Slabaugh, 1990)
		238		CPX G1L	7.0e-148	166/189	87	(Goebel <i>et al.</i> , 1990)
CSL		251		VAR-I	6.6e-147	184/200	92	(Safronov <i>et al.</i> , 1996)
				(Shchelkunov <i>et al.</i> , 1995)				
030L	26501	147	16.2	dUTPase				
F2L	26058	147		VAC	2.9e-102	147/147	100	(Roseman and Slabaugh, 1990)
		147		CPX G2L	8.2e-100	144/147	97	(Goebel <i>et al.</i> , 1990)
C6L		147		VAR	1.1e-97	142/147	96	(Safronov <i>et al.</i> , 1996)
		164		human dUTPase	4.1e-61	49/69	71	(Shchelkunov <i>et al.</i> , 1995)
				(Ladner <i>et al.</i> , 1996)				

-32-

GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START STOP	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>d</sup> expect	BLAST <sup>d</sup> AA id	HSS <sup>e</sup> (%)	references
left terminal region:								
	--142			Swinepox virus	8.0e-56	43/70	61	(Massung et al., 1993)
	159			orf virus	1.5e-49	45/69	65	(Mercer et al., 1989)
	178			avian adenovirus	6.6e-49	40/70	57	(Akopian et al., 1992)
	1124			FIV pol polyprotein dUTPase pyrophosphatase family	1.5e-26	49/117	41	(Talbott et al., 1989)
					>4.2e-06			
<b>031L</b>	<b>27955</b>	<b>476</b>	<b>55.3</b>	<b>kelch-like protein</b>				(Senkevich et al., 1993b)
	<b>26525</b>							(Roseman and Slabaugh, 1990)
<b>F3L</b>	<b>480</b>			VAC	0.0	<b>292/294</b>	<b>99</b>	(Goebel et al., 1990)
	<b>485</b>			CPX G3L	0.0	<b>287/293</b>	<b>97</b>	(Safronov et al., 1996)
<b>C7L</b>	<b>179</b>			VAR-I	1.9e-124	<b>166/179</b>	<b>92</b>	(Shchelkunov et al., 1995)
	<b>500</b>			Swinepox virus protein C13	4.4e-46	<b>39/133</b>	<b>29</b>	(Massung et al., 1993)
	<b>564</b>			VAC A55R	2.8e-12	<b>17/51</b>	<b>33</b>	(Goebel et al., 1990)
	<b>689</b>			kelch protein D.melanogaster	5.3e-18	<b>21/65</b>	<b>32</b>	(Xue and Cooley, 1993)
	<b>512</b>			CPX D18L	1.4e-16	<b>15/33</b>	<b>45</b>	(Safronov et al., 1996)
	<b>512</b>			VAC C2L	1.6e-16	<b>15/33</b>	<b>45</b>	(Goebel et al., 1990)
	<b>625</b>			T27E9.4 C. elegans	3.7e-14	<b>15/59</b>	<b>25</b>	Z82059
	<b>624</b>			human KIAA0132 protein	1.9e-13	<b>13/60</b>	<b>21</b>	D50922 o.k
	<b>817</b>			R09A8.3 (C. elegans)	1.1e-12	<b>17/45</b>	<b>37</b>	(Wilson et al., 1994)
	<b>611</b>			C47D12.7 (C. elegans)	2.4e-12	<b>22/91</b>	<b>24</b>	(Wilson et al., 1994)
	<b>530</b>			Swinepox virus	3.0e-09	<b>14/58</b>	<b>24</b>	(Massung et al., 1993)
	<b>589</b>			M M <sup>m</sup> actin binding protein	1.9e-09	<b>18/88</b>	<b>20</b>	U65079
	<b>521</b>			CPX C3L	1.2e-08	<b>15/37</b>	<b>40</b>	(Safronov et al., 1996)
	<b>509</b>			Myxoma virus MT-9	2.5e-08	<b>17/58</b>	<b>29</b>	(Upton et al., 1990a)
	<b>202</b>			Murine IAP-promoted placenta (MIPP) expressed protein	4.3e-08	<b>17/56</b>	<b>30</b>	(Chang-Yeh et al., 1991)
	<b>326</b>			A. thaliana hyp. protein	3.9e-06	<b>22/80</b>	<b>27</b>	Z99708
	<b>559</b>			Ectromelia virus p65	9.0e-6	<b>12/31</b>	<b>38</b>	(Senkevich et al., 1993b)
	<b>916</b>			$\beta$ -scrub (L. polyphemus)	0.00016	<b>13/42</b>	<b>30</b>	(Way et al., 1995)
	<b>172</b>			VAR-I J8R (BSH: J6R)	0.018	<b>15/36</b>	<b>41</b>	(Shchelkunov et al., 1995)
<b>032L</b>	<b>28925</b>	<b>319</b>	<b>37.0</b>	<b>ribonucleotide reductase (small subunit)</b>				(Slabaugh et al., 1988)
	<b>27966</b>			CPX G4L	2.3e-231	<b>317/319</b>	<b>99</b>	(Roseman and Slabaugh, 1990)
<b>F4L</b>	<b>319</b>			VAC	3.5e-231	<b>317/319</b>	<b>99</b>	(Safronov et al., 1996)
<b>C8L</b>	<b>333</b>			VAR-BSH	4.1e-228	<b>313/319</b>	<b>98</b>	(Goebel et al., 1990)
				ribonucleotide reductase family	>2.2e-10			(Shchelkunov et al., 1995)
<b>033L</b>	<b>29250</b>	<b>97</b>	<b>11.1</b>	<b>36.5k major membrane protein precursor (f1)</b>				(Roseman and Slabaugh, 1990)
	<b>28957</b>			VAR-BSH	1.9e-36	<b>51/53</b>	<b>96</b>	
<b>C9L</b>	<b>348</b>			CPX GSL	2.4e-19	<b>47/77</b>	<b>61</b>	(Shchelkunov et al., 1995)
	<b>323</b>			VAC	3.3e-19	<b>42/70</b>	<b>60</b>	(Safronov et al., 1996)
<b>F5L</b>	<b>321</b>			non-receptor tyrosin kinase (Dictyostelium discoideum)	0.00038	<b>15/35</b>	<b>42</b>	(Goebel et al., 1990)
	<b>1584</b>			36.5k major membrane protein precursor (f2)				(Tan and Spudich, 1990)
<b>034L</b>	<b>29875</b>	<b>218</b>	<b>24.8</b>					(Roseman and Slabaugh, 1990)
	<b>29219</b>			CPX GSL	8.2e-155	<b>215/217</b>	<b>99</b>	
<b>F5L</b>	<b>323</b>			VAC	6.4e-155	<b>215/217</b>	<b>99</b>	(Safronov et al., 1996)
<b>C9L</b>	<b>348</b>			VAR-BSH	6.8e-141	<b>186/210</b>	<b>88</b>	(Goebel et al., 1990)
								(Shchelkunov et al., 1995)
<b>035L</b>	<b>30129</b>	<b>74</b>	<b>8.6</b>	<b>8.6k protein</b>				(Roseman and Slabaugh, 1990)
<b>F6L</b>	<b>29905</b>	<b>74</b>		VAC	5.5e-47	<b>74/74</b>	<b>100</b>	(Goebel et al., 1990)
<b>C10L</b>	<b>72</b>			VAR	2.3e-38	<b>62/70</b>	<b>88</b>	(Shchelkunov et al., 1995)
<b>036L</b>	<b>30387</b>	<b>80</b>	<b>9.4</b>	<b>9.4k protein</b>				(Roseman and Slabaugh, 1990)
<b>C11L</b>	<b>30145</b>	<b>79</b>		VAR	2.9e-44	<b>34/43</b>	<b>79</b>	(Shchelkunov et al., 1995)
<b>F7L</b>	<b>92</b>			VAC	1.9e-43	<b>65/65</b>	<b>100</b>	(Goebel et al., 1990)
<b>037L</b>	<b>30731</b>	<b>65</b>	<b>7.9</b>	<b>7.9k protein</b>				(Roseman and Slabaugh, 1990)
<b>F8L</b>	<b>30534</b>	<b>65</b>		VAC	5.1e-43	<b>63/65</b>	<b>96</b>	(Goebel et al., 1990)
<b>C12L</b>	<b>65</b>			VAR-I	3.1e-41	<b>61/65</b>	<b>93</b>	(Shchelkunov et al., 1995)
<b>038L</b>	<b>31429</b>	<b>212</b>	<b>23.8</b>	<b>23.8k protein</b>				(Roseman and Slabaugh, 1990)
<b>F9L</b>	<b>30791</b>	<b>212</b>		VAC	7.1e-148	<b>212/212</b>	<b>100</b>	(Goebel et al., 1990)
<b>C13L</b>	<b>212</b>			VAR	1.2e-144	<b>207/212</b>	<b>97</b>	(Shchelkunov et al., 1995)
	<b>215</b>			Swinepox virus	8.1e-72	<b>39/93</b>	<b>41</b>	(Massung et al., 1993)
<b>MC016L</b>	<b>213</b>			MCV subtype 1	2.8e-62	<b>71/152</b>	<b>46</b>	(Senkevich et al., 1996)
	<b>225</b>			Orf virus	5.1e-39	<b>27/84</b>	<b>32</b>	(Mercer et al., 1995)
	<b>243</b>			FPV protein FP2	2.8e-17	<b>26/58</b>	<b>44</b>	(Binns et al., 1988)
	<b>243</b>			MCV subtype 1 MC069R	7.7e-12	<b>23/58</b>	<b>39</b>	(Senkevich et al., 1996)
	<b>250</b>			VAC L1R	1.1e-07	<b>20/58</b>	<b>34</b>	(Goebel et al., 1990)
	<b>250</b>			VAR M1R	1.1e-07	<b>20/58</b>	<b>34</b>	(Shchelkunov et al., 1995)
<b>039L</b>	<b>32735</b>	<b>439</b>	<b>52.1</b>	<b>serine/threonine protein kinase 2</b>				(Lin and Broyles, 1994)
	<b>31416</b>			VAC	0.0	<b>429/439</b>	<b>97</b>	(Wang and Shuman, 1995)
<b>F10L</b>	<b>439</b>			VAR-BSH	0.0	<b>424/439</b>	<b>96</b>	(Goebel et al., 1990)
<b>C14L</b>	<b>439</b>			Swinepox virus	2.2e-233	<b>151/214</b>	<b>70</b>	(Shchelkunov et al., 1995)
<b>MC017L</b>	<b>440</b>			MCV subtype 1	2.3e-198	<b>178/282</b>	<b>63</b>	(Massung et al., 1993)
	<b>443</b>			orf virus	2.2e-162	<b>198/366</b>	<b>54</b>	(Senkevich et al., 1996)
	<b>498</b>							(Mercer et al., 1995)
<b>040L</b>	<b>33012</b>	<b>84</b>	<b>9.6</b>	<b>39.7k protein (f1)</b>				
<b>C15L</b>	<b>32758</b>	<b>354</b>		VAR	6.6e-27	<b>50/64</b>	<b>78</b>	(Shchelkunov et al., 1995)
<b>F11L</b>	<b>354</b>			VAC	9.1e-27	<b>50/64</b>	<b>78</b>	(Goebel et al., 1990)
<b>041L</b>	<b>33771</b>	<b>100</b>	<b>11.4</b>	<b>39.7k protein (f2)</b>				

ORF <sup>a</sup>	START STOP	AA <sup>b</sup>	kDa <sup>c</sup>	name / function / homologues <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
<b>left terminal region:</b>								
<i>F11L</i>	33469	354		VAC	3.8e-62	95/95	100	(Goebel <i>et al.</i> , 1990).
<i>C15L</i>		354		VAR	8.8e-58	90/95	94	(Shchelkunov <i>et al.</i> , 1995)
<i>042L</i>	35721	635	73.1	73.1k protein	0.0	629/635	99	(Goebel <i>et al.</i> , 1990),
<i>F12L</i>	33814	635		VAC	0.0	607/635	95	(Shchelkunov <i>et al.</i> , 1995)
<i>C16L</i>		635		VAR-I	3.6e-84	28/66	42	U43549
		352		Myxoma virus	4.0e-60	29/82	35	(Senkevich <i>et al.</i> , 1996)
<i>MC019L</i>		663		MCV subtype 1	4.8e-39	19/61	31	U34774
		640		orf virus	2.3e-15	19/67	28	(Ogawa <i>et al.</i> , 1993)
		630		FPV F12 homolog				
<i>043L</i>	36866	372	41.8	37k major EEV antigen				(Hirt <i>et al.</i> , 1986)
	35748			IMCBH sensitive protein				(Schmutz <i>et al.</i> , 1991)
<i>F13L</i>		372		palmitylprotein	2.1e-268	369/372	99	(Grosenbach <i>et al.</i> , 1997)
<i>C17L</i>		372		VAC	8.9e-265	364/372	97	(Goebel <i>et al.</i> , 1990)
		371		VAR-BSH	2.5e-115	110/200	55	(Shchelkunov <i>et al.</i> , 1995)
		378		Myxoma virus	7.6e-108	83/194	42	U43549
<i>MC021L</i>		388		orf virus	6.1e-98	44/113	38	(Sullivan <i>et al.</i> , 1994)
		377		MCV subtype 1	2.8e-88	47/112	41	(Senkevich <i>et al.</i> , 1996)
		251		FPV major env protein	1.8e-62	47/112	41	(Calvert <i>et al.</i> , 1992)
		424		pigeonpox virus	2.1e-18	16/52	30	S27933
		424		CPX M4L	1.7e-17	14/35	40	(Safronov <i>et al.</i> , 1996)
		372		VAC K4L	1.4e-16	28/84	33	(Goebel <i>et al.</i> , 1990)
		437		D. discoideum	1.5e-11	25/94	26	(Giorda <i>et al.</i> , 1989)
				HU-K4 (homo sapiens)				U60644
<i>044L</i>	37105	73	8.3	8.3k protein				
<i>F14L</i>	36884	73		VAC	2.3e-44	72/73	98	(Goebel <i>et al.</i> , 1990)
<i>C18L</i>		73		VAR	2.1e-35	57/73	78	(Shchelkunov <i>et al.</i> , 1995)
<i>045L</i>	378533	158	18.6	18.6k protein				
<i>F15L</i>	37377	158		VAC	2.3e-112	157/158	99	(Goebel <i>et al.</i> , 1990),
<i>C19L</i>		161		VAR	1.4e-107	150/153	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC025L</i>		148		MCV subtype 1	3.5e-54	52/113	46	(Senkevich <i>et al.</i> , 1996)
		148		Myxoma virus	5.4e-50	48/112	42	U43549
<i>046L</i>	38555	231	26.5	26.5k protein				
<i>F16L</i>	37860	231		VAC	3.3e-159	227/231	98	(Goebel <i>et al.</i> , 1990),
<i>C20L</i>		231		VAR	5.6e-157	222/231	96	(Shchelkunov <i>et al.</i> , 1995)
		209		Myxoma virus	8.3e-48	26/58	44	U43549
<i>MC029L</i>		230		MCV subtype 1	6.9e-45	16/61	26	(Senkevich <i>et al.</i> , 1996)
<i>047R</i>	38619	101	11.3	11k DNA binding				
	38924			phosphoprotein				(Bertholet <i>et al.</i> , 1985)
<i>F17R</i>		101		VAC	3.0e-69	100/101	99	(Kao and Bauer, 1987)
<i>C21R</i>		101		VAR	9.7e-67	99/101	98	(Goebel <i>et al.</i> , 1990)
		102		MXX	6.6e-26	45/92	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC030R</i>		92		MCV subtype 1	1.5e-20	33/53	48	U43549
		46		orf virus	1.3e-06	16/29	62	(Senkevich <i>et al.</i> , 1997)
<i>048L</i>	40360	479	55.6	poly(A) polymerase				(Gershon <i>et al.</i> , 1991)
	38921			catalytic subunit				
<i>E1L</i>		479		VAC	0.0	478/479	99	(Goebel <i>et al.</i> , 1990),
<i>E1L</i>		479		VAR-I	0.0	472/479	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC031L</i>		470		MCV subtype 1	1.5e-177	114/173	65	(Senkevich <i>et al.</i> , 1997)
<i>049L</i>	42570	737	85.9	85.9k protein				
<i>E2L</i>	40357	737		VAC	0.0	735/737	99	(Ahn <i>et al.</i> , 1990a)
<i>E2L</i>		737		VAR-I	0.0	731/737	99	(Goebel <i>et al.</i> , 1990),
<i>MC032L</i>		748		MCV subtype 1	8.3e-127	59/198	29	(Shchelkunov <i>et al.</i> , 1995)
							(Senkevich <i>et al.</i> , 1997)	
<i>050L</i>	43269	190	21.5	dsRNA dependent PK				
	42697			inhibitor, host range				(Chang <i>et al.</i> , 1992)
<i>E3L</i>		190		VAC	1.4e-129	188/190	98	(Chang <i>et al.</i> , 1995b)
<i>E3L</i>		192		VAR-BSH	8.6e-126	111/114	97	(Goebel <i>et al.</i> , 1990),
		1175		dsRNA specific ADA (rat)	7.2e-12	22/47	46	(Shchelkunov <i>et al.</i> , 1995)
		1226		dsRNA specific ADA (human)	2.8e-09	21/47	44	(O'Connell <i>et al.</i> , 1995)
		551		human protein kinase p68	3.8e-05	22/42	52	(Kim <i>et al.</i> , 1994)
				INF inducible kinase family	>0.00099			(Meurs <i>et al.</i> , 1990)
<i>051L</i>	44103	259	29.8	RNA polymerase subunit				
	43324			rpo30, VITE-1				(Ahn <i>et al.</i> , 1990a)
<i>E4L</i>		259		VAC	1.6e-182	258/259	99	(Broyles and Pennington, 1990)
<i>E4L</i>		259		VAR-BSH	3.2e-180	255/259	98	(Goebel <i>et al.</i> , 1990)
<i>MC034L</i>		444		MCV subtype 1	1.2e-84	107/171	62	(Shchelkunov <i>et al.</i> , 1995)
		39		orf virus	6.7e-10	21/39	53	(Senkevich <i>et al.</i> , 1996)
		243		African swine fever virus	0.00034	17/36	47	(Mercer <i>et al.</i> , 1995)
				TFIIS family	<0.0096			(Vydelingum <i>et al.</i> , 1993)
<i>052R</i>	44180	331	39.1	39.1k protein				
<i>ESR</i>	45175	331		VAC	1.2e-235	329/331	99	(Goebel <i>et al.</i> , 1990)
<i>ESR</i>		341		VAR	3.1e-223	312/331	94	(Goebel <i>et al.</i> , 1990)
		332		Taterapox	7.1e-225	300/314	95	(Shchelkunov <i>et al.</i> , 1995)
		329		Camelpox	1.4e-221	206/220	93	(Douglas and Dumbell, 1996)
		319		Cowpox	1.5e-202	271/303	89	(Douglas and Dumbell, 1996)
		256		Ectromelia	3.8e-153	218/245	88	(Douglas and Dumbell, 1996)
<i>MC038R</i>		276		MCV subtype 1	8.3e-109	94/152	61	(Senkevich <i>et al.</i> , 1997)
<i>053R</i>	45312	567	66.7	66.7k protein				(Goebel <i>et al.</i> , 1990)

## GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / function / (putative) homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
left	STOP	terminal	region:					
E6R	567			VAR	0.0	555/567	97	(Shchelkunov <i>et al.</i> , 1995)
MC037R	565			MCV subtype I	7.2e-247	258/451	57	(Senkevich <i>et al.</i> , 1997)
054R	47082	166	19.5	17k myristylprotein				(Martin <i>et al.</i> , 1997)
E7R	47582	166		VAC	9.7e-116	166/166	100	(Goebel <i>et al.</i> , 1990)
E7R	60			VAR-I (BSH: E6.5R)	2.7e-36	53/60	88	(Shchelkunov <i>et al.</i> , 1995)
055R	47695	273	31.9	31.9k protein				(Earl <i>et al.</i> , 1986)
E8R	48516	273		VAC	4.5e-195	272/273	99	(Goebel <i>et al.</i> , 1990)
E8R	273			VAR	9.9e-192	266/273	99	(Shchelkunov <i>et al.</i> , 1993a),
MC038R	276			MCV subtype I	8.3e-109	94/152	97	(Senkevich <i>et al.</i> , 1997)
056L	51543	1006	116.9	DNA polymerase				(Earl <i>et al.</i> , 1986)
E9L	48523	1006		VAC	0.0	1005/10	99	(Goebel <i>et al.</i> , 1990),
E9L	1005			VAR BSH	0.0	06	98	(Shchelkunov <i>et al.</i> , 1995)
	1008			Orf virus	0.0	598/608	51	(Mercer <i>et al.</i> , 1996)
	988			FPV	0.0	199/388	60	(Binns <i>et al.</i> , 1987)
MC039L	1004			MCV subtype I	0.0	179/294	58	(Senkevich <i>et al.</i> , 1997)
	964			C. benni poxvirus	2.6e-77	175/297	34	(Mustafa and Yuen, 1991)
				DNA polymerase family	>6.0e-06	28/82		
057R	51575	95	10.9	10.9k protein				(Goebel <i>et al.</i> , 1990)
E10R	51862	95		VAC	1.2e-65	93/95	97	(Goebel <i>et al.</i> , 1990)
E10R	95			VAR	3.1e-64	90/95	100	(Shchelkunov <i>et al.</i> , 1993a)
MC040R	101			MCV subtype I	5.2e-44	58/95	94	(Senkevich <i>et al.</i> , 1997)
058L	52246	129	14.9	14.9k protein				(Goebel <i>et al.</i> , 1990)
E11L	51857	129		VAC	3.3e-89	129/129	100	(Goebel <i>et al.</i> , 1990)
E11L	129			VAR	4.2e-87	125/129	96	(Shchelkunov <i>et al.</i> , 1995)
MC041L	132			MCV subtype I	1.8e-30	31/96	32	(Senkevich <i>et al.</i> , 1997)
059L	52691	152	17.6	77.6k protein (f1)				(Goebel <i>et al.</i> , 1990)
O1L	52233	666		VAC	6.9e-101	151/152	99	(Goebel <i>et al.</i> , 1990),
Q1L	666			VAR-BSH	3.4e-92	137/152	90	(Shchelkunov <i>et al.</i> , 1995)
MC042L	783			MCV subtype I	1.5e-22	39/105	37	(Senkevich <i>et al.</i> , 1997)
				leu zipper, bipartite nuclear targeting sequence				(Goebel <i>et al.</i> , 1990)
060L	54189	405	47.4	77.6k protein (f2)				(Goebel <i>et al.</i> , 1990)
O1L	52972	666		VAC	5.8e-277	399/400	99	(Goebel <i>et al.</i> , 1990)
Q1L	666			VAR-I	1.7e-269	383/400	95	(Shchelkunov <i>et al.</i> , 1995)
MC042L	783			MCV subtype I	2.7e-51	38/104	36	(Senkevich <i>et al.</i> , 1997)
061L	54555	108	12.4	glutaredoxin 1				(Ahn and Moss, 1992a)
	54229							(Johnson <i>et al.</i> , 1991)
O2L	108			VAC	2.0e-74	108/108	100	(Goebel <i>et al.</i> , 1990)
Q2L	108			VAR	4.9e-72	104/108	96	(Shchelkunov <i>et al.</i> , 1995)
	106			human glutaredoxin	3.2e-31	49/106	46	(Fernando <i>et al.</i> , 1994)
				glutaredoxin family	>9.0e-05			
062L	55639	312	35.9	35.9k protein				(Schmitt and Stunnenberg, 1988)
I1L	54701	312		VAC	4.7e-208	310/312	99	(Goebel <i>et al.</i> , 1990)
K1L	312			VAR-BSH	4.8e-205	305/312	97	(Shchelkunov <i>et al.</i> , 1995)
MC044L	310			MCV subtype I	3.8e-110	163/307	53	(Senkevich <i>et al.</i> , 1996)
	1451			transcription initiation protein (S. cerevisiae)	0.029	10/28	35	(Hansen <i>et al.</i> , 1996)
063L	55867	73	8.5	8.5k protein				(Schmitt and Stunnenberg, 1988)
I2L	55646	73		VAC	5.5e-50	73/73	100	(Goebel <i>et al.</i> , 1990)
K2L	73			VAR	5.5e-50	73/73	100	(Shchelkunov <i>et al.</i> , 1995)
MC045L	72			MCV subtype I	3.5e-18	20/33	60	(Senkevich <i>et al.</i> , 1996)
	887			hypothetical yeast protein	8.1e-05	9/24	37	S48422
064L	56677	269	30.0	DNA binding phospho-protein (F4L interacting)				(Schmitt and Stunnenberg, 1988)
	55868			VAC	2.1e-173	267/269	99	(Davis and Mathews, 1993)
I3L	269			VAR	2.5e-172	265/269	98	(Goebel <i>et al.</i> , 1990)
K3L	269			MCV subtype I	9.6e-66	61/149	40	(Shchelkunov <i>et al.</i> , 1995)
MC046L	288			FPV I3 protein	8.4e-35	23/66	34	(Senkevich <i>et al.</i> , 1996)
	209							A48563
065L	59075	771	87.8	ribonucleotide reductase (large subunit)				(Schmitt and Stunnenberg, 1988)
	56760			VAC	0.0	771/771	100	(Tengelsen <i>et al.</i> , 1988)
I4L	771			VAR	0.0	761/771	98	(Goebel <i>et al.</i> , 1990)
K4L	771			ribonucleotide red. family	>1.8e-05			(Shchelkunov <i>et al.</i> , 1995)
066L	59342	79	8.8	8.8k protein				(Schmitt and Stunnenberg, 1988)
I5L	59103	79		VAC	6.3e-49	79/79	100	(Goebel <i>et al.</i> , 1990)
K5L	79			VAR	1.2e-47	76/79	96	(Shchelkunov <i>et al.</i> , 1995)
MC047L	82			MCV subtype I	2.6e-17	27/73	36	(Senkevich <i>et al.</i> , 1996)
	81			FPV 9.1k protein	1.4e-12	13/38	34	(Binns <i>et al.</i> , 1988)
	321			formate dep. nitrit reductase protein (H. influenzae)	0.00022	7/18	38	(Fleischmann <i>et al.</i> , 1995)
	496			permease (b. subtilis)	0.00031	12/43	27	gi:2415386
067L	60509	382	43.5	43.5k protein				(Schmitt and Stunnenberg, 1988)
	59361			VAC	8.6e-268	382/382	100	(Goebel <i>et al.</i> , 1990)
I6L	382			VAR	3.1e-267	380/382	99	(Shchelkunov <i>et al.</i> , 1995)
K6L	382			MCV subtype I	2.1e-99	44/119	36	(Senkevich <i>et al.</i> , 1996)
MC048L	406							

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
left terminal	STOP	region:						
		390		FPV 16 protein mitochondrial energy transfer proteins signature	1.4e-86	50/136	36	E48563, P12925 (Goebel et al., 1990)
068L	61773	423	49.0	core protein, topoisomerase II				(Schmitt and Stunnenberg, 1988)
<i>I7L</i>	60502	423		VAC	0.0	420/423	99	(Kane and Shuman, 1993)
<i>K7L</i>		423		VAR	1.5e-306	419/423	99	(Goebel et al., 1990)
MC049L		515		MCV subtype 1	1.9e-199	126/207	60	(Shchelkunov et al., 1995)
		421		FPV 17 protein	8.1e-180	185/340	54	(Senkevich et al., 1996)
		464		Amsacta moorei poxvirus	3.2e-14	14/47	29	F48563 (Hall and Moyer, 1991)
069R	61776	676	77.6	NPH-II, NTPase, RNA helicase				(Shuman, 1992),
<i>J8R</i>	63809	676		VAC	0.0	674/676	99	(Koonin and Senkevich, 1992)
<i>K8R</i>		676		VAR	0.0	665/676	98	(Goebel et al., 1990)
MC050R		684		MCV subtype 1	7.6e-227	144/272	52	(Shchelkunov et al., 1995)
		682		FPV virus 18FPV	4.2e-206	98/178	55	(Senkevich et al., 1997)
				61 matches mainly to RNA helicase family	<0.38			(Binns et al., 1988)
070L	65588	591	68.0	68k protein				(Schmitt and Stunnenberg, 1988)
<i>G1L</i>	63813	591		VAC	0.0	590/591	99	(Goebel et al., 1990)
<i>H1L</i>		591		VAR-1	0.0	582/591	98	(Shchelkunov et al., 1995)
MC056L		593		MCV subtype 1	1.2e-217	183/361	50	(Senkevich et al., 1997)
		341		FPV	9.4e-75	45/101	44	H48563
071L	65920	111	12.8	12.8k protein				(Schmitt and Stunnenberg, 1988)
<i>G3L</i>	65585	111		VAC	7.6e-74	111/111	100	(Meis and Condit, 1991)
<i>H3L</i>		111		VAR	2.4e-71	108/111	97	(Goebel et al., 1990)
MC057L		108		MCV subtype 1	0.00012	15/45	33	(Shchelkunov et al., 1995)
								(Senkevich et al., 1997)
072R	65914	220	25.8	IBT-dependent protein				(Meis and Condit, 1991)
<i>G2R</i>	66576	220		VAC	1.9e-155	220/220	100	(Goebel et al., 1990)
<i>H2R</i>		220		VAR	1.1e-151	214/220	97	(Shchelkunov et al., 1995)
MC058R		246		MCV subtype 1	2.7e-36	42/135	31	(Senkevich et al., 1997)
073L	66920	124	14.0	glutaredoxin 2 membrane protein				(Gvakharia et al., 1996)
<i>G4L</i>	66546	124		VAR	4.0e-83	123/124	99	(Jensen et al., 1996)
<i>H4L</i>		124		VAC	7.5e-83	123/124	99	(Shchelkunov et al., 1995)
MC059L		126		MCV subtype 1	1.1e-21	21/51	41	(Goebel et al., 1990)
								(Senkevich et al., 1997)
074R	66923	434	49.9	49.8k protein				(Goebel et al., 1990)
<i>G5R</i>	68227	434		VAC	1.6e-305	432/434	99	(Goebel et al., 1990)
<i>HSR</i>		434		VAR	1.9e-299	423/434	97	(Shchelkunov et al., 1995)
MC60R		437		MCV subtype 1	1.0e-55	56/119	47	(Senkevich et al., 1997)
		1300		HS CG1 protein	0.015	22/82	26	(Print et al., 1994)
075R	68235	63	7.3	RNA polymerase subunit				(Amegadzie et al., 1992),
<i>G5.5R</i>	68426	63		Vpo7				(Meis and Condit, 1991)
<i>HS.5R</i>		63		VAC	1.1e-40	63/63	100	(Goebel et al., 1990)
MC061R		63		VAR	1.1e-39	61/63	96	(Shchelkunov et al., 1995)
				MCV subtype 1	9.3e-27	41/63	65	(Senkevich et al., 1997)
				35 matches mainly to RNA polymerases	<0.54			
076R	68428	165	19.0	18.9k protein				(Goebel et al., 1990)
<i>G6R</i>	68925	165		VAC	3.8e-116	162/165	98	(Goebel et al., 1990)
<i>H6R</i>		165		VAR	1.5e-116	164/165	99	(Shchelkunov et al., 1995)
MC062R		195		MCV subtype 1	3.0e-32	27/57	47	(Senkevich et al., 1997)
077L	70005	371	42.0	42.0k protein				(Schmitt and Stunnenberg, 1988)
<i>G7L</i>	68890	371		VAC	5.2e-255	370/371	99	(Goebel et al., 1990)
<i>H7L</i>		371		VAR	7.1e-255	369/371	99	(Shchelkunov et al., 1995)
MC065L		402		MCV subtype 1	2.0e-109	69/145	47	(Senkevich et al., 1997)
078R	70036	260	29.9	VLTF-1, late transcription factor				(Keck et al., 1990)
<i>G8R</i>	70818	260		VAC	8.6e-184	259/260	99	(Wright et al., 1991)
<i>H8R</i>		260		VAR-I	3.1e-183	258/260	99	(Goebel et al., 1990)
MC067R		260		MCV subtype 1	8.5e-136	185/260	71	(Shchelkunov et al., 1995)
		260		FPV virus FPO	3.3e-129	175/250	67	(Senkevich et al., 1997)
								(Binns et al., 1988)
079R	70838	340	38.9	37k myristylprotein				(Martin et al., 1997)
<i>G9R</i>	71860	340		VAC	3.7e-237	317/319	99	(Goebel et al., 1990)
<i>H9R</i>		340		VAR	9.1e-236	315/319	98	(Shchelkunov et al., 1995)
MC068R		342		MCV subtype 1	4.8e-79	59/127	46	(Senkevich et al., 1997)
		336		FPV virus FPI	3.9e-65	59/124	47	(Binns et al., 1988)
080R	71861	250	27.3	25k myristylprotein				(Franke et al., 1990)
<i>L1R</i>	72613	250		IMV virion protein	1.8e-175	250/250	100	(Martin et al., 1997)
<i>M1R</i>		250		VAC	6.4e-170	249/250	99	(Goebel et al., 1990)
MC069R		243		VAR	6.5e-103	145/243	59	(Shchelkunov et al., 1995)
		243		MCV subtype 1	6.2e-95	128/243	52	(Senkevich et al., 1997)
		212		FPV virus FP2	1.6e-07	20/58	34	(Binns et al., 1988)
		212		VAC F9L	3.1e-07	20/58	34	(Goebel et al., 1990)
		212		VAR C13L				(Shchelkunov et al., 1995)

-36-

GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA Id	HSS <sup>f</sup> (%)	references
left terminal region:								
		213		MCV subtype I MC016L	1.6e-0.7	13/57	22	(Senkevich <i>et al.</i> , 1997)
		215		swinepox	3.3e-0.5	15/51	29	(Massung <i>et al.</i> , 1993)
081R	72645	87	10.3	10.3k protein				
L2R	72908	87		VAC	3.9e-57	87/87	100	(Plucienniczak <i>et al.</i> , 1985)
M2R		87		VAR	4.0e-56	85/87	97	(Goebel <i>et al.</i> , 1990)
MC070R		93		MCV subtype I	0.064	18/80	22	(Shchelkunov <i>et al.</i> , 1995)
		504		Na <sup>+</sup> dependent phosphate transporter <i>C. elegans</i>	6.9e-05	10/39	25	(Senkevich <i>et al.</i> , 1997)
		233		ATPase subunit <i>T. cruzi</i>	0.013	16/44	36	(Wilson <i>et al.</i> , 1994)
		2336		Ca <sup>2+</sup> channel rat	5.2e+0.2	6/25	24	(U38184)
		2238		Ca <sup>2+</sup> channel mouse	7.1e+0.2	6/25	24	(Dubel <i>et al.</i> , 1992)
		1559		ABC transporter yeast	0.40	12/40	30	(Coppola <i>et al.</i> , 1994)
								X97560
082L	73950	350	40.6	40.6k protein				
L3L	72898	350		VAC	2.2e-251	346/350	98	(Plucienniczak <i>et al.</i> , 1985)
M3L		349		VAR	1.5e-241	296/306	96	(Goebel <i>et al.</i> , 1990)
MC072L		310		MCV subtype I	1.5e-88	64/136	47	(Shchelkunov <i>et al.</i> , 1995)
		301		FPV F4 protein	1.1e-80	58/134	43	(Senkevich <i>et al.</i> , 1997)
								(Binns <i>et al.</i> , 1988)
083R	73975	251	28.5	core protein VP8				
L4R	74730			DNA/RNA binding protein				
M4R		251		VAC	5.6e-170	251/251	100	(Yang and Bauer, 1988)
MC073R		251		VAR	3.7e-169	250/251	99	(Baylis and Smith, 1997)
		254		MCV subtype I	1.7e-76	36/59	61	(Goebel <i>et al.</i> , 1990)
		253		FPV virus FPs	6.4e-55	29/57	50	(Shchelkunov <i>et al.</i> , 1995)
								(Senkevich <i>et al.</i> , 1997)
								(Binns <i>et al.</i> , 1988)
084R	74740	128	15.1	15.1k protein				
L5R	75126	128		VAC 14.0k protein	2.9e-89	127/128	99	(Goebel <i>et al.</i> , 1990)
M5R		128		VAR	2.0e-87	125/128	97	(Shchelkunov <i>et al.</i> , 1995)
MC074R		129		FPV FP6	8.1e-16	19/45	42	(Drillien <i>et al.</i> , 1987)
		146		MCV subtype I	0.073	10/18	55	(Senkevich <i>et al.</i> , 1997)
		152		melatonin receptor <i>D. rerio</i>	0.44	15/66	222	(Reppert <i>et al.</i> , 1995)
085R	75083	153	17.9	dimeric virion protein				
J1R	75544	153		VAC	6.0e-103	152/153	99	(Holzer & Falkner, unpubl.)
L1R		159		VAR-I	1.4e-101	149/153	97	(Goebel <i>et al.</i> , 1990)
		147		capripox CF7	6.5e-54	53/90	58	(Shchelkunov <i>et al.</i> , 1995)
		148		myxoma MF7	4.8e-51	54/93	58	(Gershon and Black, 1989b)
		183		MCV subtype I	1.9e-47	47/93	50	(Jackson and Bults, 1992)
MC075R		148		FPV FP7	1.3e-35	37/84	44	(Senkevich <i>et al.</i> , 1997)
								(Drillien <i>et al.</i> , 1987)
086R	75560	177	20.0	thymidine kinase				
J2R	76093	177		VAC	5.7e-125	175/177	98	(Hruby and Ball, 1982)
L2R		177		VAR	2.7e-122	170/177	96	(Weir and Moss, 1983)
				38 matches mainly to thymidine kinase family	<0.18			(Goebel <i>et al.</i> , 1990)
								(Shchelkunov <i>et al.</i> , 1995)
087R	76159	333	38.9	poly(A) polymerase subunit 2'methyl transferase				
J3R	77160			VAC	8.7e-136	330/333	99	(Gershon <i>et al.</i> , 1991)
L3R		333		VAR-BSH	9.8e-233	326/333	97	(Gershon and Moss, 1993)
MC076R		338		myxoma	5.7e-288	247/333	74	(Goebel <i>et al.</i> , 1990)
		343		MCV subtype I	1.4e-135	79/144	54	(Shchelkunov <i>et al.</i> , 1995)
		308		FPV VP39	1.7e-96	125/267	46	(Senkevich <i>et al.</i> , 1997)
								(Binns <i>et al.</i> , 1988)
088R	77075	185	21.3	RNA pol subunit rpo22				
J4R	77632	185		VAC	1.2e-125	185/185	100	(Broyles and Moss, 1986)
L4R		185		VAR-BSH	7.9e-125	182/185	98	(Goebel <i>et al.</i> , 1990)
MC077R		185		myxoma	1.5e-86	124/185	67	(Shchelkunov <i>et al.</i> , 1995)
		187		MCV subtype I	1.9e-76	73/132	55	(Jackson and Bults, 1990)
		186		FPV	2.1e-73	72/135	53	(Senkevich <i>et al.</i> , 1997)
								(Binns <i>et al.</i> , 1988)
089L	78101	133	15.2	15.2k protein				
J5L	77700	133		VAC	2.4e-95	133/133	100	(Plucienniczak <i>et al.</i> , 1985)
LSL		133		VAR-I	2.4e-94	131/133	98	(Goebel <i>et al.</i> , 1990)
MC078L		134		MCV subtype I	5.7e-45	60/127	47	(Shchelkunov <i>et al.</i> , 1995)
		137		FPV	1.4e-43	60/130	46	(Senkevich <i>et al.</i> , 1997)
		377		VAR-I A16L (BSH:A17L)	0.049	7/28	25	(Drillien <i>et al.</i> , 1987)
		378		VACA16L	0.049	7/28	25	(Shchelkunov <i>et al.</i> , 1995)
								(Goebel <i>et al.</i> , 1990)
090R	78207	1286	146.9	RNA pol subunit rpo147				
J6R	82067	1286		VAC	0.0	1283/1286	99	(Broyles and Moss, 1986)
L6R		1286		VAR	0.0	1275/1286	99	(Goebel <i>et al.</i> , 1990)
MC079R		1289		MCV subtype I	0.0	556/760	73	(Shchelkunov <i>et al.</i> , 1995)
				100 matches to RNA pol (large subunit) family	<3.7e-07			(Senkevich <i>et al.</i> , 1997)
091L	82579	171	19.7	protein tyrosine/serine phosphatase				
H1L	82064	171		VAC	2.0e-117	170/171	99	(Rosel <i>et al.</i> , 1986)
III		171		VAR	1.1e-114	166/171	97	(Guan <i>et al.</i> , 1991)
		171		raccoonpox	6.0e-111	157/171	91	(Goebel <i>et al.</i> , 1990)
		172		myxoma virus	1.5e-77	83/138	60	(Shchelkunov <i>et al.</i> , 1995)
		173		rabbit fibroma virus	1.8e-77	46/80	57	(Mossman <i>et al.</i> , 1995a)
MC082L		169		MCV subtype I	1.4e-65	60/114	52	(Mossman <i>et al.</i> , 1995b)
				protein phosphatase family	>2.8e-05			(Senkevich <i>et al.</i> , 1997)

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
	left terminal	region:						
092R	82593	189	21.5	21.5k protein				
H2R	83162	189		VAC	5.2e-134	188/189	99	(Rosel <i>et al.</i> , 1986)
12R		189		VAR	1.4e-133	188/189	99	(Goebel <i>et al.</i> , 1990)
MC083R		191		MCV subtype 1	1.4e-71	95/181	52	(Shchelkunov <i>et al.</i> , 1995)
		142		myxoma	1.3e-65	93/142	65	(Senkevich <i>et al.</i> , 1997)
								(Jackson and Bull, 1990)
093L	84139	324	37.5	immunodominant env protein p35; IMV membrane-associated				
	83165			VAC	3.3e-231	322/324	99	(Rosel <i>et al.</i> , 1986)
H3L		324		VAR-BSH	1.7e-225	311/320	97	(Chertov <i>et al.</i> , 1991)
I3L		325		MCV subtype 1	1.1e-36	38/117	32	(Takahashi <i>et al.</i> , 1994)
MC084L		298						(Goebel <i>et al.</i> , 1990)
								(Shchelkunov <i>et al.</i> , 1995)
094L	86527	795	93.6	RAP 94 (RNA-pol assoc. transcr. spec. factor)				
	84140			VAC	0.0	791/795	99	(Senkevich <i>et al.</i> , 1996)
H4L		795		VAR	0.0	780/795	98	(Ahn and Moss, 1992b)
I4L		795		MCV subtype 1	0.0	327/546	59	(Kane and Shuman, 1992)
MC085L		791		Orf virus	0.0	96/131	73	(Shchelkunov <i>et al.</i> , 1995)
		804		FPV L1L protein	2.4e-181	91/176	51	(Fleming <i>et al.</i> , 1993)
		484						2209386A
095R	86713	203	22.3	late transcription factor VLTF-4				
	87324			VAC	1.8e-128	202/203	99	(Kovacs and Moss, 1996)
HSR		203		VAR	5.1e-102	91/97	93	(Rosel <i>et al.</i> , 1986)
ISR		221		orf virus F3R	3.1e-14	29/69	42	(Goebel <i>et al.</i> , 1990)
		227		MCV subtype 1	3.1e-09	28/64	43	(Shchelkunov <i>et al.</i> , 1995)
		220		nucleolin Xenopus	0.00041	18/57	31	(Senkevich <i>et al.</i> , 1997)
		705		31 matches to glu/aspartate rich proteins	E<0.52			(Messmer and Dreyer, 1993)
096R	87325	314	36.7	DNA topoisomerase I				
	88269			VAC	0.0	314/314	100	(Shuman and Moss, 1987)
H6R		314		VAR-BSH	9.5e-220	312/314	99	(Rosel <i>et al.</i> , 1986)
I6R		314		shape fibroma virus	8.5e-141	119/170	70	(Goebel <i>et al.</i> , 1990)
		314		orf virus	5.2e-128	82/138	59	(Shchelkunov <i>et al.</i> , 1995)
MC087R		318		MCV subtype 1	1.6e-121	111/202	54	(Fleming <i>et al.</i> , 1993)
		323		FPV L3R	2.9e-113	159/303	52	(Senkevich <i>et al.</i> , 1997)
		316		21 matches to topoisomerase family				(Zantinge <i>et al.</i> , 1996)
097R	88306	146	17.0	17.0k protein				
H7R	88746	146		VAC	2.1e-98	144/146	98	(Rosel <i>et al.</i> , 1986)
I7R		146		VAR	6.7e-96	141/146	96	(Goebel <i>et al.</i> , 1990)
MC088R		143		MCV subtype 1	4.3e-30	45/115	39	(Shchelkunov <i>et al.</i> , 1995)
								(Senkevich <i>et al.</i> , 1997)
098R	88790	844	96.8	mRNA capping enzyme, large subunit				
	91324			VAC	0.0	842/844	99	(Morgan <i>et al.</i> , 1984)
D1R		844		VAR-BSH	0.0	830/844	98	(Niles <i>et al.</i> , 1986)
F1R		844		MCV subtype 1	0.0	322/64	64	(Goebel <i>et al.</i> , 1990)
MC090R		950		shape fibroma virus	0.0	243/305	79	(Shchelkunov <i>et al.</i> , 1995)
		836		ASV NP868R	0.0033	17/55	30	(Senkevich <i>et al.</i> , 1997)
		868						(Upton <i>et al.</i> , 1991b)
								(Pena <i>et al.</i> , 1993)
099L	91723	146	16.9	structural protein				
	91283			VAC	5.9e-98	146/146	100	(Niles <i>et al.</i> , 1986)
D2L		146		VAR (BSH; F3L)	1.5e-97	145/146	99	(Dyster and Niles, 1991)
F2L		146		Rabbit fibroma virus	2.0e-27	13/33	39	(Goebel <i>et al.</i> , 1990)
MC091L		143		MCV subtype 1	1.1e-20	19/41	46	(Shchelkunov <i>et al.</i> , 1995)
		170						(Senkevich <i>et al.</i> , 1996)
100R	91716	233	27.6	27k structural protein				
D3R	92417	237		VAC	3.8e-167	136/142	95	(Dyster and Niles, 1991)
F2R		237		VAR I:F3R	1.5e-162	131/142	92	(Goebel <i>et al.</i> , 1990)
		241		shape fibroma virus	9.3e-20	27/100	27	(Shchelkunov <i>et al.</i> , 1995)
MC092R		268		MCV subtype 1	3.5e-18	16/39	41	(Upton <i>et al.</i> , 1991b)
		206		rabbit fibroma virus C3	1.6e-09	26/96	27	(Senkevich <i>et al.</i> , 1997)
								(Strayer <i>et al.</i> , 1991)
101R	92417	218	25.1	uracil DNA glycosylase				
D4R	93073	218		VAC	1.4e-157	217/218	99	(Upton <i>et al.</i> , 1993)
F4R		218		VAR-BSH	5.1e-157	216/218	99	(Goebel <i>et al.</i> , 1990)
		218		shape fibroma virus	1.5e-117	151/218	69	(Shchelkunov <i>et al.</i> , 1995)
MC093R		226		MCV subtype 1	8.4e-91	65/113	57	(Upton <i>et al.</i> , 1993)
		218		FPV FPD4	3.1e-88	116/216	53	(Senkevich <i>et al.</i> , 1997)
		297		uracil DNA glycosylase UL2	0.019	8/14	57	(Tartaglia <i>et al.</i> , 1990)
				gallid herpesvirus 1				L34064
102R	93105	785	90.4	90.4k ATP/GTP binding protein				
	95462			VAC	0.0	780/785	99	(Niles <i>et al.</i> , 1986)
D5R		785		VAR	0.0	774/785	98	(Shchelkunov <i>et al.</i> , 1993c)
FSR		785		shape fibroma C5	0.0	283/450	62	(Goebel <i>et al.</i> , 1990)
		786		MCV subtype 1	0.0	184/334	55	(Shchelkunov <i>et al.</i> , 1995)
		791		FPV virus FPD5	0.0	170/345	49	(Senkevich <i>et al.</i> , 1997)
MC094R		791		C29E6.4 C. elegans	0.72	16/56	28	(Tartaglia <i>et al.</i> , 1990)
		942						(Wilson <i>et al.</i> , 1994)
103R	95503	637	73.9	early transcription factor VETF-1				
	97416							(Bryoles and Fesler, 1990)
								(Gershon and Moss, 1990)

-38-

GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START STOP	AA <sup>b</sup>	kDa <sup>c</sup>	name / function / (putative) homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
left terminal		region:						
<i>D6R</i>	637	VAC		0.0	635/637	99	(Goebel <i>et al.</i> , 1990)	
<i>F6R</i>	637	VAR-I		0.0	633/637	99	(Shchelkunov <i>et al.</i> , 1995)	
<i>MC095R</i>	635	shepe fibroma virus		0.0	212/262	80	(Strayer <i>et al.</i> , 1991)	
	635	MCV subtype I		0.0	199/263	75	(Senkevich <i>et al.</i> , 1997)	
	605	FPV		0.0	188/263	71	(Binns <i>et al.</i> , 1990)	
	648	Choristoneura biennis EPV	2.7e-08	24/72	33	(Tartaglia <i>et al.</i> , 1990)		
<i>104R</i>	648	Amsacta moorei EPV	4.2e-06	24/77	31	(Yuen <i>et al.</i> , 1991)		
	706	African swine fever virus	1.5e-05	13/38	34	(Hall and Moyer, 1991)		
	97443	RNA polymerase subunit rpo18					(Yanez <i>et al.</i> , 1993)	
<i>D7R</i>	161	VAC	1.4e-108	160/161	99	(Ahn <i>et al.</i> , 1990b)		
<i>F7R</i>	161	VAR	2.2e-106	156/161	96	(Quick and Broyles, 1990)		
<i>MC097R</i>	163	rabbit fibroma C8	3.4e-76	108/161	67	(Goebel <i>et al.</i> , 1990)		
	161	MCV subtype I	4.0e-70	99/158	62	(Shchelkunov <i>et al.</i> , 1995)		
	161	FPV D7	5.4e-66	95/160	59	(Senkevich <i>et al.</i> , 1997)		
<i>105L</i>	98805	virion transmembrane protein, carbonic anhydrase-like					(Binns <i>et al.</i> , 1990)	
<i>D8L</i>	304	VAC	2.3e-212	297/304	97	(Niles and Seto, 1988)		
	304	VAR	2.5e-209	291/304	95	(Niles <i>et al.</i> , 1986)		
	304	Camelpox virus	1.1e-207	290/304	95	(Maa <i>et al.</i> , 1990)		
	303	Ectromelia virus	2.2e-207	195/207	94	(Goebel <i>et al.</i> , 1990)		
	304	Monkeypox virus	3.0e-207	287/304	94	(Shchelkunov <i>et al.</i> , 1995)		
	304	Cowpox virus	9.8e-206	285/304	93	(X97857)		
		Carbonic anhydrase family	>4.9e-13			(X97856)		
<i>106R</i>	98847	25k mutT-like protein					(X97855)	
<i>D9R</i>	213	VAC	1.6e-146	212/213	99	(X97858)		
	213	VAR	5.3e-145	209/213	98	(Koonin, 1993)		
	218	rabbit fibroma	1.7e-75	105/203	51	(Niles <i>et al.</i> , 1986)		
<i>MC098R</i>	212	MCV subtype I	5.3e-67	54/111	48	(Goebel <i>et al.</i> , 1990)		
	78	FPV D9	2.0e-13	25/51	49	(Shchelkunov <i>et al.</i> , 1995)		
	229	MCV subtype I	0.0041	13/31	41	(Tartaglia <i>et al.</i> , 1990)		
<i>MC099R</i>	248	VAR-I F10R	0.018	14/32	43	(Senkevich <i>et al.</i> , 1997)		
	225	FPV D10	0.14	15/34	44	(Shchelkunov <i>et al.</i> , 1995)		
	248	VAC D10R	0.23	11/26	42	(Tartaglia <i>et al.</i> , 1990)		
<i>107R</i>	99485	29k mutT-like protein					(Goebel <i>et al.</i> , 1990)	
<i>D10R</i>	248	VAC	7.4e-173	245/248	98	(Koonin, 1993)		
	248	VAR-I	5.4e-173	245/248	98	(Niles <i>et al.</i> , 1986)		
	260	shepe fibroma D10	3.8e-72	96/202	47	(Goebel <i>et al.</i> , 1990)		
	229	MCV subtype I	1.4e-54	44/100	44	(Shchelkunov <i>et al.</i> , 1995)		
	225	FPV D10	1.1e-45	45/102	44	(Strayer <i>et al.</i> , 1991)		
	218	shepe fibroma D9	1.9e-06	19/54	35	(Senkevich <i>et al.</i> , 1997)		
	212	MCV subtype I MC098R	0.13	12/21	57	(Binns <i>et al.</i> , 1990)		
	136	mutator Synechocystis	0.23	12/27	44	(Strayer <i>et al.</i> , 1991)		
	213	VAC D9R	0.24	11/26	42	(Senkevich <i>et al.</i> , 1997)		
	213	VAR F9R	0.24	11/26	42	(D90899)		
<i>N1L</i>	169	mutator <i>M. jannaschii</i>	0.39	13/25	52	(Shchelkunov <i>et al.</i> , 1995)		
						(Bult <i>et al.</i> , 1996)		
<i>108L</i>	102127	nuclcoside triphosphate phosphohydrolyase I, DNA helicase					(Broyles and Moss, 1987)	
<i>D11L</i>	631	VAC	0.0	629/631	99	(Rodriguez <i>et al.</i> , 1986)		
	631	VAR	0.0	626/631	99	(Koonin and Senkevich, 1992)		
	634	MCV subtype I	7.3e-286	392/627	62	(Goebel <i>et al.</i> , 1990)		
	637	FPV protein S	2.8e-275	214/357	59	(Shchelkunov <i>et al.</i> , 1995)		
	370	Rabbit fibroma C14 protein	1.8e-176	244/368	66	(Senkevich <i>et al.</i> , 1996)		
	648	AmEPV	6.0e-142	81/159	50	S42251		
	648	Choristoneura biennis EPV	1.1e-136	81/158	51	F36819		
	89	Swinepox virus	1.2e-34	60/89	67	(Hall and Moyer, 1991)		
	1098	ASF	1.6e-13	26/89	29	(Yuen <i>et al.</i> , 1991)		
	1085	RAD26 (yeast)	5.1e-05	16/45	35	(Massung <i>et al.</i> , 1993)		
	769	HS transcription activator	0.00093	10/22	45	(Baylis <i>et al.</i> , 1993)		
		NTPase family	>5.1e-5			(Huang <i>et al.</i> , 1994)		
						(Okabe <i>et al.</i> , 1992)		
<i>109L</i>	103025	mRNA capping enzyme, transcription initiation factor VIIF					(Niles <i>et al.</i> , 1989)	
<i>D12L</i>	287	VAC	2.0e-198	285/287	99	(Weinrich and Hruby, 1986)		
	287	VAR	9.8e-198	284/287	99	(Vos <i>et al.</i> , 1991)		
	287	Swinepox virus	4.1e-160	220/287	76	(Goebel <i>et al.</i> , 1990)		
	295	MCV subtype I	5.8e-126	171/279	61	(Shchelkunov <i>et al.</i> , 1995)		
	289	FPV protein 6	3.4e-113	114/215	53	(Massung <i>et al.</i> , 1993)		
<i>110L</i>	104711	rifampicin resistance gene, IMV protein					(Senkevich <i>et al.</i> , 1996)	
<i>D13L</i>	551	VAC	0.0	551/551	100	(Tartaglia and Paoletti, 1985)		
	551	VAR	0.0	547/551	99	(Weinrich and Hruby, 1986)		
	551	Swinepox virus	4.5e-286	357/506	70	(Goebel <i>et al.</i> , 1990)		
	547	MCV subtype I	5.4e-248	298/494	60	(Shchelkunov <i>et al.</i> , 1995)		
	552	FPV protein 7	6.6e-223	182/305	59	(Massung <i>et al.</i> , 1993)		
	584	Heliothis armigera EPV	9.5e-51	54/107	50	(Senkevich <i>et al.</i> , 1996)		

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
<b>left terminal region:</b>								
111L	105187	150	16.9	late gene trans-activator, VLTF-2				(Weinrich and Hruby, 1986)
	104735							(Keck <i>et al.</i> , 1993)
A1L		150		VAC	6.8e-103	149/150	99	(Goebel <i>et al.</i> , 1990)
A1L		150		VAR	6.8e-103	149/150	99	(Shchelkunov <i>et al.</i> , 1995)
MC103L		169		MCV subtype I	6.3e-54	74/147	50	(Senkevich <i>et al.</i> , 1996)
		154		FPV protein 8	2.8e-50	50/87	57	S42254
112L	105882	224	26.3	late gene trans-activator				(Weinrich and Hruby, 1986)
A2L	105208			VAC				(Passarelli <i>et al.</i> , 1996)
A2L		224		VAR	1.3e-158	224/224	100	(Goebel <i>et al.</i> , 1990)
MC104L		224		MCV subtype I	1.3e-158	224/224	100	(Shchelkunov <i>et al.</i> , 1995)
		228		orf virus	6.4e-127	172/222	77	(Senkevich <i>et al.</i> , 1996)
		606			6.8e-30	43/66	65	(Mercer <i>et al.</i> , 1995)
113L	106109	76	8.9	8.9k protein				(Weinrich and Hruby, 1986)
	105879	76		VAC-WR	1.6e-47	73/76	96	
A3L		76		VAR-BSH (I:A2.5L)	2.1e-47	71/76	93	(Shchelkunov <i>et al.</i> , 1995)
MC105L		70		MCV subtype I	9.8e-12	26/63	41	(Senkevich <i>et al.</i> , 1996)
114L	108058	644	72.6	major core protein P4b				(Rosel and Moss, 1985)
A3L	106124	644		VAC	0.0	643/644	99	(Goebel <i>et al.</i> , 1990)
A4L		644		VAR-BSH (I:A3L)	0.0	636/644	98	(Shchelkunov <i>et al.</i> , 1995)
MC106L		675		MCV subtype I	8.9e-272	227/357	63	(Senkevich <i>et al.</i> , 1996)
		657		FPV Major core protein P4b	9.1e-220	169/299	56	(Binns <i>et al.</i> , 1989)
115L	108929	272	29.9	membrane associated core protein				(Dermkowicz <i>et al.</i> , 1992)
	108111			VAC	1.1e-145	180/187	96	(Cudinore <i>et al.</i> , 1996)
A4L		281		VAR-BSH (I: A4L)	1.1e-112	165/178	92	(Goebel <i>et al.</i> , 1990)
ASL		271		Thermoproteus phage 1	1.9e-09	38/127	29	(Shchelkunov <i>et al.</i> , 1995)
		268		human mucin	4.5e-07	34/139	24	(Neumann and Zillig, 1990)
		5179		many matches to Pro-rich proteins				(Gum <i>et al.</i> , 1994)
116R	108967	164	19.0	RNA pol subunit rpo19				(Ahn <i>et al.</i> , 1992)
A5R	109461	164		VAC	5.8e-110	164/164	100	(Goebel <i>et al.</i> , 1990)
A5R		164		VAR-I (BSH:A6R)	7.0e-109	162/164	98	(Shchelkunov <i>et al.</i> , 1995)
MC108R		165		MCV subtype I	3.3e-51	82/151	53	(Senkevich <i>et al.</i> , 1997)
		167		FPV	3.3e-51	72/161	44	(Kumar and Boyle, 1990)
				54 matches/glu-rich proteins	<0.51			
117L	110576	372	43.1	43.1k protein				(Goebel <i>et al.</i> , 1990)
A6L	109458	372		VAC	1.2e-248	371/372	99	(Shchelkunov <i>et al.</i> , 1995)
A7L		372		VAR-BSH (I: A6L)	1.1e-244	364/372	97	(Senkevich <i>et al.</i> , 1996)
MC109L		461		MCV subtype I	4.0e-99	132/367	35	B60013
		339		FPV ORF 2 protein	1.9e-95	111/279	39	
118L	112732	710	82.3	VETF 82k subunit				(Gershon and Moss, 1990)
A7L	110600	710		VAC	0.0	708/710	99	(Goebel <i>et al.</i> , 1990)
A8L		710		VAR-BSH (I: A7L)	0.0	700/710	98	(Shchelkunov <i>et al.</i> , 1995)
MC110L		707		MCV subtype I	0.0	240/374	64	(Senkevich <i>et al.</i> , 1996)
119R	112786	288	33.6	33.6k protein				(Van Meir and Wittek, 1988)
A8R	113652	288		VAC	5.3e-198	287/288	99	(Goebel <i>et al.</i> , 1990)
A8R		288		VAR-I (BSH:A9R)	3.1e-195	284/288	98	(Shchelkunov <i>et al.</i> , 1995)
MC111R		435		MCV subtype I	4.4e-94	100/169	59	(Senkevich <i>et al.</i> , 1997)
120L	113929	94	10.5	10.5k protein				(Van Meir and Wittek, 1988)
A10L	113645	95		VAR-BSH (I: A9L)	9.0e-59	78/79	98	(Shchelkunov <i>et al.</i> , 1995)
A9L		99		VAC	9.4e-55	82/91	90	(Goebel <i>et al.</i> , 1990)
MC112L		128		MCV subtype I	1.0e-29	47/71	66	(Senkevich <i>et al.</i> , 1996)
		69		orf virus	3.0e-16	27/45	60	(Mercer <i>et al.</i> , 1995)
121L	116605	891	102.2	major core protein P4a				(Van Meir and Wittek, 1988)
	113930			VAC	0.0	883/891	99	(Vanslyke <i>et al.</i> , 1991)
A10L		891		VAR-BSH (I: A10L)	0.0	442/463	95	(Goebel <i>et al.</i> , 1990)
A11L		892		MCV subtype I	5.8e-289	99/177	55	(Shchelkunov <i>et al.</i> , 1995)
MC113L		889						(Senkevich <i>et al.</i> , 1996)
122R	116620	318	36.1	36.1k protein				(Goebel <i>et al.</i> , 1990)
A11R	117576	318		VAC	3.5e-212	318/318	100	(Shchelkunov <i>et al.</i> , 1995)
A11R		319		VAR-I (BSH: A12R)	2.7e-154	242/277	87	(Senkevich <i>et al.</i> , 1997)
MC114R		304		MCV subtype I	2.9e-98	92/154	59	A20158
		148		FPV 4a gene	1.9e-13	18/32	56	
123L	118141	187	20.0	virion protein				(Takahashi <i>et al.</i> , 1994)
A12L	117578	192		VAC	4.8e-127	127/128	99	(Goebel <i>et al.</i> , 1990)
A13L		189		VAR-BSH (I: A12L)	5.9e-64	101/144	70	(Shchelkunov <i>et al.</i> , 1995)
MC115L		178		MCV subtype I	5.9e-37	39/83	46	(Senkevich <i>et al.</i> , 1996)
124L	118377	70	7.6	structural protein				(Takahashi <i>et al.</i> , 1994)
	118165			IMV membrane protein				(Jensen <i>et al.</i> , 1996)
		70		p 8	2.4e-42	66/69	95	(Goebel <i>et al.</i> , 1990)
A13L		68		VAC	4.1e-20	37/64	57	(Shchelkunov <i>et al.</i> , 1995)
A14L				VAR-BSH (I: A13L)				
125L	118757	90	10.0	structural protein				(Takahashi <i>et al.</i> , 1994)
	118485			IMV membrane protein				(Jensen <i>et al.</i> , 1996)
				p 16				

-40-  
GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA Id	HSS <sup>f</sup> (%)	references
<b>left terminal regions:</b>								
A14L	90			VAC	5.3e-62	90/90	100	(Goebel <i>et al.</i> , 1990)
A15L	90			VAR-BSH (l: A14L)	5.3e-61	88/90	97	(Shchelkunov <i>et al.</i> , 1995)
MC118L	94			MCV subtype 1	7.3e-22	31/72	43	(Senkevich <i>et al.</i> , 1996)
	125			human interferon inducible protein	0.23	15/49	30	(Deblandre <i>et al.</i> , 1995)
126L	119209	94	11.0	11k protein				
A15L	118925	94		VAC	4.1e-63	94/94	100	(Goebel <i>et al.</i> , 1990)
A16L	94			VAR-BSH (l: A15L)	1.0e-61	92/94	97	(Shchelkunov <i>et al.</i> , 1995)
MC120L	96			MCV subtype 1	6.7e-08	17/51	33	(Senkevich <i>et al.</i> , 1996)
127L	120326	377	43.4	35k myristylprotein				
A16L	119193	378		VAC	6.3e-288	327/327	100	(Martin <i>et al.</i> , 1997)
A17L	377			VAR-BSH (l: A16L)	1.5e-283	368/377	97	(Goebel <i>et al.</i> , 1990)
MC121L	364			MCV subtype 1	6.5e-110	45/115	39	(Shchelkunov <i>et al.</i> , 1995)
128L	120940	203	23.0	IMV membrane protein morphogenesis factor				(Senkevich <i>et al.</i> , 1996)
	120329							(Krijnse-Locker <i>et al.</i> , 1996)
								(Rodriguez <i>et al.</i> , 1995)
A17L	203			VAC	1.0e-141	201/203	99	(Wolffe <i>et al.</i> , 1996)
A18L	203			VAR-BSH (l: A17L)	1.0e-141	201/203	99	(Goebel <i>et al.</i> , 1990)
MC122L	179			MCV subtype 1	1.4e-47	36/81	44	(Shchelkunov <i>et al.</i> , 1995)
129R	120955	493	56.8	DNA helicase				(Senkevich <i>et al.</i> , 1996)
	122436			DNA dependent ATPase				(Koonin and Senkevich, 1992)
A18R	493			VAC	0.0	488/493	98	(Bayliss and Condit, 1995)
A18R	493			VAR-I (BSH:A19R)	0.0	478/493	96	(Goebel <i>et al.</i> , 1990)
MC123R	694			MCV subtype 1	5.3e-167	203/403	50	(Shchelkunov <i>et al.</i> , 1995)
	450			Bacteriophage T3 D10 helicase-like protein	0.0066	13/36	36	(Senkevich <i>et al.</i> , 1997)
130L	122650	77	8.3	8.3kb protein				P11107
A19L	122417	77		VAC	2.9e-50	77/77	100	(Goebel <i>et al.</i> , 1990)
A19L	76			VAR-I (BSH: A20L)	1.2e-34	54/64	84	(Goebel <i>et al.</i> , 1990)
MC124L	78			MCV subtype 1	1.5e-13	14/37	37	(Shchelkunov <i>et al.</i> , 1995)
	1721			HS RIZ, zink finger protein	0.0060	7/16	43	(Senkevich <i>et al.</i> , 1996)
131L	123004	117	13.6	13.6k protein				(Buyse <i>et al.</i> , 1995)
A21L	122651	117		VAC	5.3e-83	117/117	100	(Goebel <i>et al.</i> , 1990)
A22L	117			VAR-BSH (l: A20L)	7.2e-82	115/117	98	(Goebel <i>et al.</i> , 1990)
MC125L	114			MCV subtype 1	2.8e-28	23/41	56	(Shchelkunov <i>et al.</i> , 1995)
132R	123003	426	49.1	49.1k protein				(Senkevich <i>et al.</i> , 1996)
A20R	124283	426		VAC	7.6e-298	423/426	99	(Goebel <i>et al.</i> , 1990)
A21R	426			VAR	1.6e-294	418/426	98	(Goebel <i>et al.</i> , 1990)
MC126R	476			MCV subtype 1	3.2e-95	34/131	25	(Shchelkunov <i>et al.</i> , 1995)
	1118			Pichia klyveri DNA pol	0.069	12/54	22	(Senkevich <i>et al.</i> , 1997)
133R	124213	187	21.9	21.9k protein				Y11606
A22R	124776	187		VAR-I (BSH:A23R)	1.1e-126	182/187	97	(Goebel <i>et al.</i> , 1990)
A22R	176			VAC	1.2e-122	174/176	98	(Shchelkunov <i>et al.</i> , 1995)
MC127R	282			MCV subtype 1	5.8e-43	35/85	41	(Senkevich <i>et al.</i> , 1997)
134R	124796	382	44.6	44.6k protein				(Goebel <i>et al.</i> , 1990)
A23R	125944	382		VAC	4.2e-269	382/382	100	(Goebel <i>et al.</i> , 1990)
A23R	382			VARI (BSH:A24R)	1.7e-265	377/382	98	(Shchelkunov <i>et al.</i> , 1995)
MC128R	383			MCV subtype 1	3.5e-136	83/143	58	(Senkevich <i>et al.</i> , 1997)
135R	125966	1155	132.4	RNA pol subunit rpo132				(Hooda-Dhingra <i>et al.</i> , 1990)
	129436							(Amegadzie <i>et al.</i> , 1991b)
A24R	1164			VAC	0.0	794/796	99	(Goebel <i>et al.</i> , 1990)
	1164			CPX rpo132	0.0	794/795	99	(Patel and Pickup, 1989)
A25R	1164			VAR-BSH (l: A24R)	0.0	789/795	99	(Shchelkunov <i>et al.</i> , 1995)
MC129R	1165			MCV subtype 1	0.0	441/565	78	(Senkevich <i>et al.</i> , 1997)
	1162			orf virus	0.0	166/258	64	U33419
				101 matches to RNA pol beta subunit family	<0.036			
<b>right terminal regions:</b>								
136L	129638	65	7.5	150k CPX-ATI (f)				(Funahashi <i>et al.</i> , 1988)
A25L	129441	65		VAC	1.3e-41	64/65	98	(Goebel <i>et al.</i> , 1990)
	1284			Cowpox (CPX-ATI)	3.2e-15	28/30	93	(Funahashi <i>et al.</i> , 1988)
137L	130916	230	27.1	27.1k protein (f)				(Amegadzie <i>et al.</i> , 1991a)
A30L	130224	498		VAR-BSH (l: A29L)	3.1e-158	216/227	95	(Shchelkunov <i>et al.</i> , 1995)
A26L	322			VAC (ATI flanking protein)	5.6e-142	195/197	98	(Goebel <i>et al.</i> , 1990)
MC131L	513			MCV subtype 1	2.1e-12	19/59	32	(Senkevich <i>et al.</i> , 1996)
MC133L	546			MCV subtype 1	4.2e-11	12/40	30	(Senkevich <i>et al.</i> , 1996)
MC130L	451			MCV subtype 1	2.3e-10	14/40	35	(Senkevich <i>et al.</i> , 1996)
	702			VAR-I A28L (BSH:A29L)	0.0021	12/37	32	(Shchelkunov <i>et al.</i> , 1995)
	726			Camelpox	0.051	11/37	29	(Meyer and Rziha, 1993)
138L	131298	110	12.5	14k membrane protein				(Rodriguez and Esteban, 1987)
	130966			EEV protein				(Rodriguez and Smith, 1990)
				fusion protein				(Gong <i>et al.</i> , 1990)
A27L	110			VAC	3.3e-70	108/110	98	(Goebel <i>et al.</i> , 1990)
A31L	110			VAR-BSH (l: /A30L)	1.1e-69	107/110	97	(Shchelkunov <i>et al.</i> , 1995)
	117			Camelpox virus	1.5e-69	106/110	96	(Meyer <i>et al.</i> , 1994)
	110			Cowpox virus	1.6e-69	107/110	97	(Meyer <i>et al.</i> , 1994)

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA Id	HSS <sup>f</sup> (%)	references
left terminal region:								
		110		Ectromelia virus	6.7e-68	105/110	95	(Meyer <i>et al.</i> , 1994)
		110		Monkeypox virus	8.3e-67	103/110	93	(Meyer <i>et al.</i> , 1994)
		89		Orf virus	4.8e-15	22/57	38	(Naase <i>et al.</i> , 1991)
		188		Myxoma virus	2.5e-12	18/33	54	(Jackson <i>et al.</i> , 1996)
MC133L		546		MCV subtype 1	1.5e-11	26/58	44	(Senkevich <i>et al.</i> , 1996)
MC131L		148		Capripox virus HM2 protein	2.6e-10	21/42	50	(Gershon <i>et al.</i> , 1989)
		513		MCV subtype 1	1.5e-05	18/58	31	(Senkevich <i>et al.</i> , 1996)
139L	131739	146	16.3	16.3k protein				
A28L	131299	146		VAC	1.7e-103	146/146	100	(Amegadzie <i>et al.</i> , 1991a)
A31.5L		146		VAR-BSH (I: A31L)	2.9e-100	141/146	96	(Goebel <i>et al.</i> , 1990)
		140		Myxoma virus	1.3e-55	30/52	57	(Shchelkunov <i>et al.</i> , 1995)
MC134L		140		Capripox virus HM3 protein	3.3e-55	30/49	61	(Jackson <i>et al.</i> , 1996)
		141		MCV subtype 1	1.0e-53	31/52	59	(Gershon <i>et al.</i> , 1989)
		143		Amsacta moorei poxvirus	2.0e-14	16/36	44	(Senkevich <i>et al.</i> , 1996)
140L	132657	305	35.4	RNA pol subunit rpo35				
A29L	131740	305		VAC	3.6e-215	304/305	99	(Amegadzie <i>et al.</i> , 1991a)
A32L		305		VAR-BSH	7.5e-211	297/305	97	(Goebel <i>et al.</i> , 1990)
MC135L		303		MCV subtype 1	7.0e-98	51/103	49	(Shchelkunov <i>et al.</i> , 1995)
		126		Capripox virus	2.2e-54	46/61	75	(Senkevich <i>et al.</i> , 1996)
141L	132853	77	8.7	8.7k protein				
A30L	132620	77		VAC	5.5e-48	77/77	100	(Amegadzie <i>et al.</i> , 1991a)
A33L		77		VAR	5.5e-48	77/77	100	(Goebel <i>et al.</i> , 1990)
MC136L		67		MCV subtype 1	9.2e-16	18/40	45	(Shchelkunov <i>et al.</i> , 1995)
142R	133013	125	14.4	14.4k protein				
A37R	133390	124		VAC	2.0e-84	118/124	95	(Senkevich <i>et al.</i> , 1997)
A34R		140		VAR	1.6e-79	111/114	97	(Koonin <i>et al.</i> , 1991)
MC138R		117		MCV subtype 1	6.2e-24	39/98	39	(Shchelkunov <i>et al.</i> , 1990)
143L	134169	269	30.8	30.8k protein				
		133360		ATP/GTP binding motif A				
A32L		300		VAC	6.4e-190	268/269	99	(Amegadzie <i>et al.</i> , 1991)
A35L		270		VAR	1.6e-186	263/269	97	(Goebel <i>et al.</i> , 1990)
MC140L		249		MCV subtype 1	7.6e-95	58/94	61	(Shchelkunov <i>et al.</i> , 1995)
144R	134287	185	20.6	EEV glycoprotein				
A33R	134844	185		VAC	2.1e-124	182/185	98	(Senkevich <i>et al.</i> , 1997)
A36R		184		VAR	1.8e-121	103/112	91	(Goebel <i>et al.</i> , 1990)
		185		Ectromelia	2.8e-113	165/185	89	(Shchelkunov <i>et al.</i> , 1995)
145R	134868	168	19.6	EEV glycoprotein				
	135374			virulence factor				
A34R		168		actin microvilli inducer				
A37R		168		VAC	1.2e-117	165/168	98	(Duncan and Smith, 1992a)
		167		VAR-I	1.7e-117	164/168	97	(McIntosh and Smith, 1996)
		199		FPV ORFs BamHI 2,8,11 hepatic lectins homologs	<0.056	16/66	24	(Wolffe <i>et al.</i> , 1997)
				HS early T-cell activation antigen CD69	0.0038	12/38	31	(Shchelkunov <i>et al.</i> , 1995)
MC143R		159		MCV subtype 1	0.080	12/48	25	(Tomley <i>et al.</i> , 1988)
				17 matches to lectins				
146R	135418	176	20.0	20.0k protein				
A35R	135948	176		VAC	1.4e-126	176/176	100	(Amegadzie <i>et al.</i> , 1991)
A38R		60		VAR-I	2.9e-37	57/60	95	(Goebel <i>et al.</i> , 1990)
MC145R		233		MCV subtype 1	1.2e-07	18/55	32	(Shchelkunov <i>et al.</i> , 1995)
147R	136015	208	23.8k	EEV membrane protein				
	136641			virulence factor				
A36R		221		VAC	2.8e-143	140/141	99	(Parkinson and Smith, 1994)
A39R		216		VAR	2.1e-89	138/177	77	(Smith <i>et al.</i> , 1991)
				19 matches to asn/ser-rich proteins	<0.41			(Goebel <i>et al.</i> , 1990)
148R	136705	263	29.8	29.8k protein				
A37R	137496	263		VAC	6.8e-183	261/262	99	(Shchelkunov <i>et al.</i> , 1995)
A40R		68		VAR	4.9e-37	61/67	91	(Goebel <i>et al.</i> , 1990)
149L	138589	277	31.5	31.5k protein				
A38L	137756	277		VAC	9.3e-198	274/277	98	(Amegadzie <i>et al.</i> , 1991a)
A41L		277		VAR	1.6e-187	259/277	93	(Goebel <i>et al.</i> , 1990)
		303		Rattus norvegicus CD47	3.9e-24	23/86	26	(Shchelkunov <i>et al.</i> , 1995)
		324		MM integrin assoc. protein	1.0e-21	23/86	26	(Nishiyama <i>et al.</i> , 1997)
		323		human CD47 precursor	5.0e-19	28/86	32	(Lindberg <i>et al.</i> , 1993)
								(Campbell <i>et al.</i> , 1992)
150R	138606	83	9.4	semaphorin-like protein (f1)				(Kolodkin <i>et al.</i> , 1993)
	138857			VAC	8.0e-46	73/76	96	
A42R		403		VAR-I	8.6e-44	67/71	94	(Shchelkunov <i>et al.</i> , 1995)
151R	139163	210	23.9	semaphorin-like protein (f2)				
	139795			VAC	3.0e-147	209/210	99	(Kolodkin <i>et al.</i> , 1993)
A39R		403		VAR (I:A44R)	1.8e-68	91/105	86	(Goebel <i>et al.</i> , 1990)
A43R		139		semaphorin-like protein	1.7e-20	29/79	36	(Shchelkunov <i>et al.</i> , 1995)
		653		Alcelaphine herpesvirus				
				37 matches to semaphorin				(Ensser and Fleckenstein, 1995)

-42-

GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologues <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references	
	left	terminal	region:	/collapsin gene family					
152R	139821	168	19.4	NK cell receptor homolog lectin-like protein				(Scheiflinger et al., unpubl.)	
	140327			VAC	6.6e-97	134/137	97	(Smith et al., 1991)	
A40R		168		VAR-I (BSH: A43.5R)	9.6e-36	54/59	91	(Goebel et al., 1990)	
A45R		61		HS natural killer (NK) cell protein group 2-A, B	4.5e-11	20/74	27	(Shchelkunov et al., 1995)	
	233			HS type II membrane protein	6.9e-11	16/36	44	(Houchins et al., 1991)	
	240			MM NK cell receptor	5.5e-09	16/36	44	(Adamkiewicz et al., 1994)	
	182			HS CD 94	1.7e-07	11/29	37	(Giorda et al., 1992)	
	179			127 matches to lectins including NK cell surface proteins and snake venoms				(Chang et al., 1995a)	
153L	141025	219	25.1	25.1k protein				(Smith et al., 1991)	
A41L	140366	219		VAC	1.9e-158	218/219	99	(Goebel et al., 1990)	
A44L		218		VAR-BSH (I: A46L)	1.4e-152	152/159	95	(Shchelkunov et al., 1995)	
	244			VAC B29R/C23L	0.0076	12/53	22	(Goebel et al., 1990)	
	258			Rabbit fibroma virus T1	0.057	13/49	26	(Upton et al., 1987)	
154R	141197	128	14.5	profilin-like protein				(Blasco et al., 1991)	
	141583			VAC				(Smith et al., 1991)	
A42R		133		VAR-I (BSH: A45R)	1.2e-87	85/87	97	(Goebel et al., 1990)	
A47R		133		HS profilin	1.4e-85	82/87	94	(Shchelkunov et al., 1995)	
	140			10 matches profilin family	2.2e-23	19/45	42	(Kwiatkowski and Bruns, 1988)	
155R	141621	190	22.1	class I membrane glycoprotein				(Smith et al., 1991)	
	142193			VAC				(Duncan and Smith, 1992b)	
A43R		194		VAR-I (BSH: A46R)	1.5e-137	162/164	98	(Goebel et al., 1990)	
A48R		195		HS leukocytic antigen	1.9e-128	101/109	92	(Shchelkunov et al., 1995)	
	51				0.096	7/23	30	X79517	
156R	142201	78	8.8	8.8k protein				(Smith et al., 1991)	
	142437	78		VAC-WR Salf6R	3.9e-45	78/78	100	(Smith et al., 1991)	
	258			rabbit myosin heavy chain	0.00048	13/39	33	A02985	
				144 matches to various asp/glu/lys-rich proteins					
157L	143577	346	39.4	3 $\beta$ -hydroxysteroid dehydrogenase (3 $\beta$ -HSD)				(Moore and Smith, 1992)	
	142537			VAC				(Blasco et al., 1991)	
A44L		346		VAR-BSH (I: A49L)	4.5e-249	342/346	98	(Goebel et al., 1990)	
A47L		210		MCV subtype I	1.1e-136	185/195	94	(Shchelkunov et al., 1995)	
MC152R		354		FPV	8.2e-104	123/272	45	(Senkevich et al., 1996)	
	369			matches to dihydroflavonol reductases, cholesterol dehydrogenases, UDP-galactose-4-epimerases	3.1e-83	33/85	38	(Skinner et al., 1994)	
					>2.8e-05			(Baker and Blasco, 1992)	
158R	143624	121	13.3	superoxide dismutase-like protein				(Blasco et al., 1991)	
	143989			VAC				(Smith et al., 1991)	
A45R		125		VAR-I BSH A48R	2.1e-82	94/96	97	(Goebel et al., 1990)	
A51R		125		117 matches with superoxide dismutase family	1.1e-82	93/96	96	(Shchelkunov et al., 1995)	
<0.027									
159R	143979	241	27.6	27.6k protein				(Smith et al., 1991)	
A46R	144701	214		VAC	9.6e-167	238/240	99	(Goebel et al., 1990)	
A52R		240		VAR-I (BSH: A49R)	5.6e-164	233/240	97	(Shchelkunov et al., 1995)	
160L	145465	238	27.6	27.6k protein				(Goebel et al., 1990)	
J1L	144749	244		VAR	5.1e-146	114/127	89	(Shchelkunov et al., 1995)	
A47L		244		VAC	8.2e-135	121/127	95	(Goebel et al., 1990)	
				integrin lipid binding motif				(Smith et al., 1991)	
161R	145564	204	23.2	thymidylate kinase				(Smith et al., 1991)	
A48R	146178	204		VAC	5.2e-140	204/204	100	(Goebel et al., 1990)	
J2R		205		VAR	1.1e-137	161/165	97	(Shchelkunov et al., 1995)	
				16 matches to thymidylate kinase family	<0.49				
162R	146202	162	18.8	18.8k protein				(Smith et al., 1991)	
A49R	146690	162		VAC	6.0e-106	159/162	98	(Goebel et al., 1990)	
J3R		162		VAR	2.4e-103	154/162	95	(Shchelkunov et al., 1995)	
163R	146722	552	63.5	DNA ligase				(Kerr and Smith, 1989)	
AS0R	148380	552		VAC	0.0	547/552	99	(Goebel et al., 1990)	
J4R		552		VAR-I	0.0	537/552	97	(Shchelkunov et al., 1995)	
	922			HS DNA ligase III	2.1e-235	102/165	61	(Wei et al., )	
	539			shape fibroma ligase	9.9e-213	95/200	47	(Parks et al., 1994)	
	564			FPV ligase	3.0e-195	101/170	59	(Skinner et al., 1994)	
				31 matches mainly to DNA ligase family	<0.029				
164R	148426	310	34.9	34.9k protein				(Antoine et al., 1996)	
AS1R	149358	334		VAC	1.5e-217	267/274	97	(Goebel et al., 1990)	
J5R		334		VAR	9.1e-208	251/274	91	(Shchelkunov et al., 1995)	

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologues <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA Id	HSS <sup>f</sup> (%)	references
left terminal region:								
				fusion of AS1R/ASSR ORFs				(Antoine <i>et al.</i> , 1996)
165R	149416	315	34.8	hemagglutinin				
AS6R	150363	315		VAC	1.8e-211	312/315	99	(Shida, 1986)
J9R		313		VAR-I(BSH:J7R)	4.3e-178	183/238	76	(Goebel <i>et al.</i> , 1990)
		310		raccoonpox	1.5e-91	74/104	71	(Shchelkunov <i>et al.</i> , 1995)
				124 matches to various proteins	<0.34			(Cavallaro and Esposito, 1992)
166R	150659	97	11.4	guanylate kinase (f)				
AS7R	150952	151		VAC	3.2e-62	94/97	96	(Smith <i>et al.</i> , 1991)
J10R		151		VAR (BSH:J8R)	2.2e-57	88/97	90	(Goebel <i>et al.</i> , 1990)
		198		MM guanylate kinase	4.3e-24	39/91	42	(Shchelkunov <i>et al.</i> , 1995)
		197		HS guanylate kinase	2.8e-20	35/91	38	(Brady <i>et al.</i> , 1996)
				21 matches mainly to guanylate kinases	<0.20			(Brady <i>et al.</i> , 1996)
167R	151103	300	34.3	serine/threonine protein kinase				
	152005							(Howard and Smith, 1989)
								(Banham and Smith, 1992)
B1R		300		VAC	7.1e-215	298/300	99	(Lin <i>et al.</i> , 1992)
B1R		300		VAR-I	2.7e-210	289/300	96	(Goebel <i>et al.</i> , 1990)
		283		VAC B12R	4.9e-49	27/53	50	(Shchelkunov <i>et al.</i> , 1995)
				100 matches mainly to protein kinase family	<0.00031			(Goebel <i>et al.</i> , 1990)
168R	152144	96	11.5	24.6k protein (f1)				
B2R	152434	219		VAC	8.5e-38	54/60	90	(Goebel <i>et al.</i> , 1990)
		149		histone H2A pea	0.59	16/50	32	P40281
169R	152289	143	16.1	24.6k protein (f2)				(Goebel <i>et al.</i> , 1990)
B2R	152720	219		VAC	5.7e-86	124/128	96	(Goebel <i>et al.</i> , 1990)
170R	152917	179	20.9	20.9k protein (f)				
B3R	153456	124		VAC	8.2e-33	51/56	91	(Goebel <i>et al.</i> , 1990)
		167		VAC WR	5.3e-45	51/56	91	(Smith <i>et al.</i> , 1991)
		92		VAR-GAR HSR	3.4e-06	19/28	67	U18339
171R	153683	177	21.4	65k ank-like protein virulence factor (f1)				
	154216			VAC	8.5e-107	151/154	98	(Howard <i>et al.</i> , 1991)
B4R		558		VAR-I (BSH:B5R)	1.7e-98	140/154	90	(Mossman <i>et al.</i> , 1996)
B6R		558		65k ank-like protein virulence factor (f2)				(Goebel <i>et al.</i> , 1990)
172R	154107	409	47.7	VAC				(Shchelkunov <i>et al.</i> , 1995)
	155336			VAR-I (BSH:B5R)	2.4e-283	195/201	97	(Howard <i>et al.</i> , 1991)
B4R		558		MM ankyrin 3	2.3e-270	185/201	92	(Mossman <i>et al.</i> , 1996)
B6R		558		orf virus	5.5e-10	19/57	33	(Shchelkunov <i>et al.</i> , 1995)
	483			VAC B18R	9.7e-10	22/54	40	(Peters <i>et al.</i> , 1995)
	1765			VAR-I B19R	1.8e-09	16/47	34	U34774
	516			HS KIAA0379	3.3e-09	11/23	47	(Goebel <i>et al.</i> , 1990)
	574			CPX host range gene	3.6e-09	19/72	26	(Shchelkunov <i>et al.</i> , 1995)
	574			VAC WR hr gene	5.1e-09	20/52	38	AB002377
	882			CPX M1L	1.7e-08	14/47	29	(Spchner <i>et al.</i> , 1988)
	668			CPX OIL	2.8e-08	15/47	31	(Kotwal and Moss, 1988a)
	237			VAR OIL	5.1e-07	23/81	28	(Goebel <i>et al.</i> , 1990)
	472			CPX DIL	8.7e-07	22/61	36	(Safronov <i>et al.</i> , 1996)
	474			VAC C9L	8.8e-07	23/81	28	(Shchelkunov <i>et al.</i> , 1995)
	446			159 matches including ankyrin proteins	1.7e-06	8/27	29	(Safronov <i>et al.</i> , 1996)
	437				7.8e-05			(Goebel <i>et al.</i> , 1990)
	634							
173R	155424	317	35.1	ps/hr protein/EEV gp42				
	156377			complement control protein				(Takahashi-Nishimaki <i>et al.</i> , 1991)
B5R		317		VAC	1.6e-232	312/317	98	(Engelstad <i>et al.</i> , 1992)
B7R		317		VAR-I (BSH:B6R)	7.1e-220	294/316	93	(Isaacs <i>et al.</i> , 1992)
	259			CPX D17L	2.1e-12	16/52	30	(Goebel <i>et al.</i> , 1990)
				186 matches to complement control protein family	<7.7e-05			(Shchelkunov <i>et al.</i> , 1995)
174R	156474	173	20.2	20.2k protein				
B6R	156995	173		VAC	1.5e-121	173/173	100	(Goebel <i>et al.</i> , 1990)
B7R		65		VAR-BSH (I:B8R)	6.0e-40	62/65	95	(Shchelkunov <i>et al.</i> , 1995)
		685		NAD-protein ADP ribosyl-transferase phage T4	0.56	17/56	30	SXBPT4
175R	157033	177	20.7	20.7k protein				
B7R	157566	182		VAC	7.8e-129	95/108	87	(Goebel <i>et al.</i> , 1990)
		184		VAC C8L	0.16	9/44	20	(Goebel <i>et al.</i> , 1990)
		182		CPX D12L	0.49	8/36	22	(Safronov <i>et al.</i> , 1996)
				EF-hand calcium-binding domain				
176R	157621	226	26.0	31k interferon-gamma receptor (f)				
	158301			VAC	3.3e-164	116/123	94	(Upton <i>et al.</i> , 1992)
B8R		272		VAR-BSH (I:B9R)	3.0e-153	111/123	90	(Alcami and Smith, 1995)
		266		ECT	2.6e-151	110/123	89	(Goebel <i>et al.</i> , 1990)
		274		swinepox C6	3.2e-09	12/31	38	(Shchelkunov <i>et al.</i> , 1995)
								(Massung <i>et al.</i> , 1993)

## GENOMIC SEQUENCE OF THE MVA STRAIN

ORF <sup>a</sup>	START STOP	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA Id	HSS <sup>f</sup> (%)	references
<b>left terminal region:</b>								
177R B9R	158458 158676	72 77 240 237	8.3	8.3k protein VAC capripox T4 protein shep fibroma virus	3.0e-49 1.2e-09 0.0057	60/60 16/44 15/50	100 36 30	(Goebel <i>et al.</i> , 1990) M28823 F43692
178R B10R	158639 159115	158 166 530 689	17.9	17.9k protein VAC swinepox VC04 kelch protein <i>D. melanogaster</i>	4.7e-110 0.040 0.14	146/146 13/42 12/54	100 30 27	(Goebel <i>et al.</i> , 1990) (Massung <i>et al.</i> , 1993) (Xue and Cooley, 1993) (Senkevich <i>et al.</i> , 1993b)
179R B11R	159187 159411	74 88	8.5	8.5k protein VAC 177 matches to glu/asn rich proteins	9.2e-43	70/73	95	(Goebel <i>et al.</i> , 1990)
180R B12R B12R	159478 160329	283 283 134 300 300	33.3	protein kinase VAC VAR-I VAC B1R VAR-I B1R 120 matches mainly to protein kinase family	1.8e-207 8.7e-26 1.7e-54 7.7e-53 <0.34	282/283 31/54 26/53 25/53	99 57 49 47	(Howard and Smith, 1989) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995)
181R B13R B13R	160437 160787	116	13.0	ICE inhibitor / SPI-2 (f1)				(Kotwal and Moss, 1989) (Smith <i>et al.</i> , 1989)
		116 344 341 353 344 357 355 372 372		VAC VAR-I (BSH:B12R) CPX crmA VAC C12L (SPI-1) Ectromelia serpin rabbitpox SPI-1 CPX SPI-1 VAR-I B25R (BSH:B21R) CPX serpin-like protein 135 matches mainly to serpins	3.0e-72 2.7e-69 2.8e-39 2.1e-23 9.2e-23 5.5e-22 1.4e-21 1.7e-21 1.7e-36	111/116 105/114 66/100 25/34 24/34 25/34 25/36 25/34 25/36	95 92 66 73 70 73 69 73 69	(Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) (Pickup <i>et al.</i> , 1986) (Goebel <i>et al.</i> , 1990) (Senkevich <i>et al.</i> , 1993b) (Ali <i>et al.</i> , 1994) (Ali <i>et al.</i> , 1994) (Shchelkunov <i>et al.</i> , 1995) (Ali <i>et al.</i> , 1994)
182R B14R	160762 161430	222	24.9	ICE inhibitor/SPI-2 (f2)				see above (Goebel <i>et al.</i> , 1990)
		345 345 341 344		VAC VAC WR rabbit pox SPI-2 CPX crmA VAR-I (BSH:B12R) 309 matches see above	6.2e-158 9.4e-156 1.6e-153 4.5e-148 1.5e-146 <1.3e-21	218/222 215/221 211/221 203/220 203/220	98 97 95 92 92	(Kotwal and Moss, 1989) (Ali <i>et al.</i> , 1994) (Pickup <i>et al.</i> , 1986) (Shchelkunov <i>et al.</i> , 1995)
183R B15R B14R	161506 161937	143 149 149	16.7	16.7k protein VAC VAR-I(BSH:B13R) VAR-I D1L (BSH:D2L) VAC C16L/B22R capripox T3A rabbit fibroma T3A VAC A52R VAC WR K7R VAR-IC4R CPX M6R	3.6e-105 9.1e-104 8.8e-31 1.0e-26 1.4e-17 2.6e-07 0.073 0.21 0.30 0.51	97/98 95/98 25/52 25/52 17/42 17/44 10/28 7/22 7/22 7/22	98 96 48 48 40 38 35 31 31 31	(Smith and Chan, 1991) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) (Shchelkunov <i>et al.</i> , 1995) (Goebel <i>et al.</i> , 1990) (Gershon and Black, 1989a) (Upton <i>et al.</i> , 1987) (Goebel <i>et al.</i> , 1990) (Boursnell <i>et al.</i> , 1988) (Shchelkunov <i>et al.</i> , 1995) (Safronov <i>et al.</i> , 1996)
184R B16R B17R	162021 163001	326	36.6	Interleukin-1 $\beta$ receptor (IL-1BR)				(Alcami and Smith, 1992) (Spriggs <i>et al.</i> , 1992)
		326 326 290 69 296		VAC-WR B15R CPX B16 VAC VAR-I (BSH:deleted) HS type II IL-1 receptor 271 matches mainly to IL-1 receptors, growth factor receptors and Ig family proteins	2.8e-229 2.3e-217 4.4e-202 8.1e-38 1.7e-36 <0.011	323/326 306/326 287/290 59/68 28/75	99 93 98 86 37	(Smith <i>et al.</i> , 1991) (Spriggs <i>et al.</i> , 1992) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) U64094
185L B17L B15L	164069 163047 340	340	39.6	39.6k protein VAC VAR-BSH (I:B18L)	4.8e-248 2.7e-241	335/340 325/340	98 95	(Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995)
186R B18R B19R	164209 165933 574	574	68.0	68k ankyrin-like protein VAC VAR-I (BSH:B16R) 100 matches mainly to poxvirus ankyrin proteins	0.0 0.0 <0.53	560/574 539/574	97 93	(Smith <i>et al.</i> , 1991) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995)
187R B19R B20R	165999 353 166703 354 569	234	27.5	surface antigen, IFN-alpha/beta receptor (f)	1.4e-163 1.53-149 0.0051 <0.53	218/233 111/133 15/43	93 83 34	(Ueda <i>et al.</i> , 1990) (Symons <i>et al.</i> , 1995) (Colamonici <i>et al.</i> , 1995) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) (McMahan <i>et al.</i> , 1991)
188R	167202	70	8.2	8.2k protein (f)				

ORF <sup>a</sup>	START	AA <sup>b</sup>	kDa <sup>c</sup>	name / (putative) function / homologies <sup>d</sup>	BLAST <sup>e</sup> expect	BLAST <sup>e</sup> AA id	HSS <sup>f</sup> (%)	references
left	STOP	terminal	region:					
B22R	167414	1897		VAR-BSH (I:B26R)	9.9e-23	31/38	81	(Shchelkunov <i>et al.</i> , 1995)
189R	167897	188	21.7	21.7k protein				
B22R	168463	181		VAC B22R/C16L	2.9e-111	95/104	91	(Goebel <i>et al.</i> , 1990)
D1L	153			VAR-I(BSH:D2L)	1.2e-88	66/71	92	(Shchelkunov <i>et al.</i> , 1995)
	149			VAC B15R	7.2e-19	25/52	48	(Goebel <i>et al.</i> , 1990)
	159			capripox T3A	8.0e-05	15/45	33	(Gershon and Black, 1989a)
	151			VAC C6L	0.25	12/46	26	(Goebel <i>et al.</i> , 1990)
	156			VAR (I:D9L;BSH:D12L)	0.26	12/46	26	(Shchelkunov <i>et al.</i> , 1995)
190R/ 004L	168531	233	26.9	45k ank-like protein (f2)				
B23R	386			VAC (C17L/B23R)	6.2e-159	110/110	100	(Goebel <i>et al.</i> , 1990)
D1L	91			VAR-BSH	9.1e-31	46/49	93	(Shchelkunov <i>et al.</i> , 1995)
	669			CPX host range	1.1e-13	22/50	44	(Spehner <i>et al.</i> , 1988)
	452			VAR-I D6L (BSH:D8L)	1.7e-11	21/50	42	(Shchelkunov <i>et al.</i> , 1995)
	574			VAR-I B19R (BSH: B16R)	1.2e-05	22/73	30	(Shchelkunov <i>et al.</i> , 1995)
	574			VAC B18R (WR: B17R)	8.6e-05	22/73	30	(Goebel <i>et al.</i> , 1990)
	634			VAC C9L	0.00011	11/24	45	(Kotwal and Moss, 1988a)
	585			VAR-I GIR	0.00013	22/74	29	(Shchelkunov <i>et al.</i> , 1995)
	516			orf virus	0.0088	15/49	30	(Sullivan <i>et al.</i> , 1995b)
	153			VAR-I D7L (BSH:D10L)	0.014	12/28	42	(Shchelkunov <i>et al.</i> , 1995)
191R/ 003L	169309	102	12.1	45k ank-like protein (f1)				
B23R	386			VAC C17L/B23R	1.3e-39	62/63	98	(Goebel <i>et al.</i> , 1990)
192R/ 002L	170303	176	19.7	secr. TNF receptor (f)				
	170835	355		CPX crmB	5.1e-71	76/83	91	(Upton <i>et al.</i> , 1991a)
G2R	348			VAR-BSH	1.0e-66	73/83	87	(Hu <i>et al.</i> , 1994)
	326			Myxoma virus T2	4.9e-30	21/37	56	(Shchelkunov <i>et al.</i> , 1995)
	325			Rabbit fibroma Virus T2	1.8e-28	17/36	47	(Upton <i>et al.</i> , 1987)
	202			CPX C4L	8.7e-15	30/51	58	(Heller <i>et al.</i> , 1990)
B25R	346			HS TNF receptor	1.9e-08	14/26	53	(Safronov <i>et al.</i> , 1996)
	259			VAC (C19L/B25R)	0.00026	16/19	84	(Goebel <i>et al.</i> , 1990)
	277			human CD40L receptor	0.0015	11/24	45	(Stamencovic <i>et al.</i> , 1989)
				30 matches to TNF receptors and surface proteins	<0.39			
193R/ 001L	171267	136	14.9	35k major secr. protein chemokine receptor (f)				
	171677			VAC (C23L/B29R)	6.0e-57	41/42	97	(Patel <i>et al.</i> , 1990)
B29R	244			VAR-I	8.9e-51	46/49	93	(Graham <i>et al.</i> , 1997)
G5R	253			CPX ORFB	5.6e-49	40/42	95	(Goebel <i>et al.</i> , 1990)
	246			SFV T1 protein	2.5e-20	23/42	54	(Shchelkunov <i>et al.</i> , 1995)
	258			Myxoma virus T1/35kDa	1.5e-14	21/42	50	(Hu <i>et al.</i> , 1994)
	260							(Upton <i>et al.</i> , 1987)
								(Graham <i>et al.</i> , 1997)

<sup>a</sup> Open reading frame coding for at least 65 amino acids (for exceptions see text); minor ORFs located in reverse orientation within large ORFs or ORFs located in the repeat regions of the ITRs (see text) are not listed; the MVA ORFs (boldface), listed consecutively as appearing in the genome, and homologs in the Copenhagen strain (in italics), in the variola strains and in the *molluscum contagiosum*, are listed in this row. Split ORFs are boxed.

<sup>b</sup> Number of deduced amino acids (AA) encoded within an ORF.

<sup>c</sup> Predicted M<sub>r</sub> (kDa) for the unmodified protein.

<sup>d</sup> The lowest Poisson probability determined by the BLAST search (Altschul *et al.*, 1990). The Expect value of 0.0 indicates a probability of zero that an alignment occurs by chance; low Expect values correspond to high homology and vice versa.

<sup>e</sup> Amino acid identity (AA id) of first high-scoring segment pair in the BLASTp protocol.

<sup>f</sup> Amino acid Identity of first high-scoring segment pair (HSS)%.

<sup>g</sup> Homologies based on searching PIR and SWISS-PROT databases (BLASTp nr).

<sup>h</sup> Duplicated ORFs located in ITRs.

<sup>i</sup> Fragment; complete homologous ORF present in related poxvirus (see reference).

<sup>j</sup> Variola India (I) or variola Bangladesh (BSH) sequences; in cases where the variola sequences are not identical, the variola strain first appearing in the blast search protocol is listed.

<sup>k</sup> ank, ankyrin.

<sup>l</sup> HS, *homo sapiens*.

<sup>m</sup> MM, *Mus musculus*.

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## GENOMIC SEQUENCE OF THE MVA STRAIN

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